

DISSERTATION

**“A COMPARATIVE STUDY OF ENTONOX WITH
EPIDURAL(0.125 % BUPIVACAINE WITH 2 µgm/ml
FENTANYL) FOR LABOUR ANALGESIA”**

submitted to

**The Tamil Nadu Dr.M.G.R Medical University
*in partial fulfillment of the
requirement for the award of the degree of***

M.D (Branch X) Anesthesiology



**Stanley Medical College
The Tamil Nadu Dr.M.G.R Medical University
Chennai, Tamil Nadu**

FEBRUARY 2006

CERTIFICATE

This is to certify that the dissertation “ **A COMPARATIVE STUDY OF ENTONOX VERSUS EPIDURAL(0.125 % BUPIVACAINE WITH 2 µgm/ml FENTANYL) FOR LABOUR ANALGESIA**” presented herein by **DR.F.MOHAMED ALI KHAN.** is an original work done in the Department of Anesthesiology, Government Stanley Medical College and Hospital, Chennai for the award of the degree of M.D. (Branch X) Anesthesiology under my guidance and supervision during the academic period of 2003-2006.

Prof.Dr.T.Raveendran.M.D.,D.T.C.D
Dean
Govt Stanley Medical
College and Hospital, Chennai

Prof.R.Meenakshi. M.D.D.A
Professor and HOD
Dept of Anesthesiology
Govt Stanley Medical College
and Hospital ,Chennai.

DECLARATION

**I, Dr. F.MOHAMED ALI KHAN solemnly declare that the dissertation titled
“COMPARATIVE STUDY : ENTONOX VERSUS EPIDURAL(0.125 %
BUPIVACAINE WITH 2 µgm/ml FENTANYL) FOR LABOUR ANALGESIA”
is a bonafide work done by me in the Department of Anesthesiology,
Stanley Medical College and Hospital, Chennai under the able guidance
of Prof.R.Meenakshi. M.D.D.A Professor and HOD, Department of
Anesthesiology, Govt. Stanley, Medical College and Hospital,
Chennai-600 001**

Place: Chennai

Date:

(Dr.F.Mohamed Ali Khan.)

ACKNOWLEDGEMENT

This study would have not been materialized, but for the patients and their relatives, hence first and foremost I would like to thank them without whom this study would not have been possible.

I wish to express my sincere thanks to **Prof.Dr.T.Raveendran, M.D., D.T.C.D.** Dean, Govt. SMC, Chennai for having permitted me to utilize the infrastructure facility of the hospital.

I am immensely grateful to **Prof R.Meenakshi, M.D.D.A**, Head of Department of Anesthesiology, SMC, Chennai who was instrumental in carrying out the study and for the constant supervision, encouragement, for providing all the necessary arrangements for the conduct of the study.

I express my grateful thanks to **Prof .Dr.Devambigai M.D., D.G.O**, Superintendent of Govt, RSRM Hospital and her faculty for the commitment and valuable co-operation.

I express my grateful thanks to **Prof .Dr.M.NAZIR AHMED M.D.D.A**, Department of Anaesthesiology, RSRM Hospital for his valuable guidance and help he rendered to me.

I am greatly indebted to **Prof.S.Dr.Nellai Kumar M.D.D.A**, Additional Professor of Anesthesiology for his valuable inputs and guidance which has gone into the making of this study.

I wish to express my sincere thanks to **Prof.Dr.C.R.Kanyakumari, M.D.D.A** for her kind and valuable assistance in performing the study.

I thank **Dr.R.S.Vijayalakshmi M.D.D.A**, Registrar for her kind help and co-operation.

I also thank **Messrs Ravishanker.M.** and **Ramanuja Rao of BOC(INDIA) LIMITED** who supplied me with the Kit and Entonox cylinders and gave me their valuable inputs.

I thank **Mr.R.Murali Krishnan** who helped us with the Statistical analysis.

I wish to express my thanks to

- All Assistant professors of Stanley Medical College and Govt. RSRM hospital.
- Theatre Personnel for their unrelenting assistance and co-operation.

I would be failing in my duty, if I don't thank my colleagues and Post graduates for their invaluable support and co-operation.

INTRODUCTION

"May no living being suffer from pain"

-Lord Buddha.

I start my study with homage to this noble sentiment.

The severity of labor pain was recognized by the Romans, who termed delivery the *poena magna*—the “great pain” or “great punishment.” Pregnancy, though is one of the most pleasant part of a woman’s life is marred by the anxious awaiting of a painful labour. Although labor is painless in a few women, the vast majority considers it painful, and a clear majority rates it as severe pain. Melzack, one of the authors of the gate control theory of pain, developed a questionnaire to assess the intensity and emotional impact of pain. Using this tool, he observed that labor pain was rated as more painful than cancer pain and that, among nulliparous women with no prepared childbirth training, it was nearly as painful as amputation of a digit without anesthesia.

IASP defines pain as “an unpleasant sensory and emotional experience associated with actual or potential tissue damage or described in terms of the actual damage.”

This definition embraces various concepts especially the subjectivity of the symptoms which is the basis of the non-pharmacological options in the treatment of labor pain.

AIM:

- To compare Entonox with Epidural Technique (0.125 % Bupivacaine with 2 µgm/ml Fentanyl) for labour analgesia in

Effectiveness of pain relief

Duration of Labour

Foetal outcome

- To study the influence on maternal and foetal parameters.

HISTORICAL PERSPECTIVES

Ancient methods of pain relief included various plant-derived sedatives, acupuncture and physical methods such as binding.

- In **1842** Crawford Long -administered Chloroform anaesthesia
- In **1847** James Young Simpson -administered the first obstetric general anaesthetic using ether.
- In **1853** John Snow -delivered Queen Victoria's eighth child under chloroform.
- In **1881** Stanislav Krikovitch- described the use of nitrous oxide for labour in Russia.
- In **1902** Morphine and hyoscine was first used in labour.
- In **1926** Gelert –administered Para-cervical block for labor pain relief.
- In **1927** Della Paine -First lumbar sympathetic block for labor pain relief
- In **1928** Cleland - Defined uterine pain pathway
- In **1931** Eugen Bogdan Aburel, Romanian obstetrician, described continuous caudal plus lumbo aortic plexus blocks in Labour.
- In **1935** Graffignere- Epidural block for labor analgesia.
- In **1949** Flower First use of continuous epidural block for obstetric analgesia

- In **1949** Cleland described continuous lumbar epidural block in labour.
- In **1950** Bromage brought an Extensive and improved understanding to epidural blockade
- In **1958** Ferdinand Lamaze published his book suggesting that pain was a conditioned reflex triggered by uterine contractions, and that psycho prophylaxis could reduce pain.

Further, advancements were made in the fields of labor analgesia to minimize the adverse effects of technique and drugs on the mother, foetus, and the labor process. This led to the following advancement

1. use of lower concentrations of the drugs
2. Use of continuous infusions of low concentrations
3. Use of Patient Controlled Analgesia technique
4. Limiting analgesia from
 - a. T10 to L1 – First stage
 - b. Sacral segments – Second stage
5. Use of Opioids combined with local anesthetic to enhance the analgesic properties.

LABOR PAIN - INCIDENCE AND ITS NEURO ANATOMY

PAIN IN THE FIRST STAGE OF LABOUR

Uterine contractions cause stretching, tearing and distortion and possibly Ischemia of the uterine tissues, whilst simultaneous dilatation of the cervix and stretching of the lower uterine segment is occurring. The intensity of the pain increases progressively with the rising strength of the contractions and these painful stimuli are transmitted by A δ and C afferent fibers which accompany sympathetic pathways through the pelvic, inferior, middle and superior hypogastric plexuses, the lumbar sympathetic chain, the white rami of the spinal nerves T10, T11, T12 and L1 and the posterior roots of these nerves to reach the spinal cord . In early labour, only the nerve roots of T11 and T12 are involved, but as the intensity of contractions increases, T10 and L1 are also recruited.

Clinical Implications—*During* the first stage of labour, an epidural block limited to the T11, T12 segments at the beginning and later extending to involve T10 and L1 will be usually sufficient to provide excellent pain relief while avoiding neural blockade of the sacral segments. Premature sacral blockade can result in the loss of the stimulating effect upon contractions of Ferguson's reflex and the loss of pelvic muscle tone which aids the rotation of the presenting part.

PAIN IN THE SECOND STAGE OF LABOUR

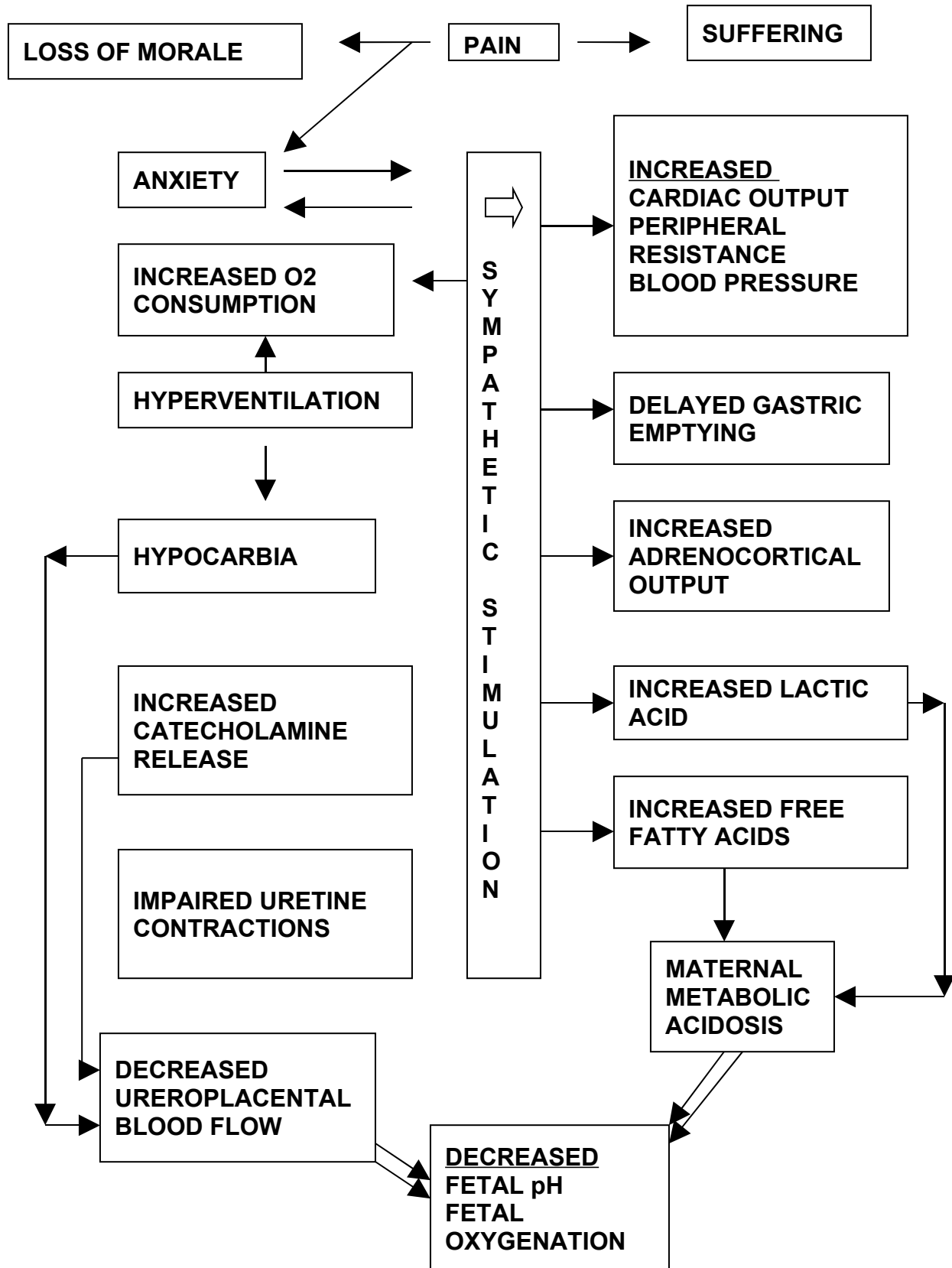
The pain caused by distension of the pelvic structure and perineum following descent of the presenting part is added to the pain of uterine contractions although, once cervical dilatation is complete, the pain induced by contractions may become less intense. The uterine pain continues to be referred to T10—L1, while the pain produced by stretching or pressure exerted

on intrapelvic structures, including the peritoneum, bladder, urethra and rectum is referred to sacral segments. Pressure on the roots of the lumbosacral plexus may manifest itself as pain felt low in the back or in the thighs. Pain produced by stretching the perineum is transmitted by the pudendal nerve (S2, 3, 4) and in part by the posterior cutaneous nerve of the thigh (S2, 3), the genitofemoral nerve (L1, 2) and the ilio-inguinal nerve (L1).

Clinical Implications: Later in the first stage and during the earlier part of the second stage, pain is often experienced in lower lumbar and upper sacral segments; so the block will have to be extended if analgesia is to be guaranteed. Complete block of the sacral segments need only be performed when perineal pain become worrisome and, by this stage, the block of the thoracolumbar segments will hopefully be decaying to such an extent that abdominal muscle strength will be adequate to permit voluntary expulsive efforts by the mother.

PAIN IN LABOUR: PATHWAYS AND MECHANISMS

<i>Site of Origin</i>	<i>Mechanism</i>	<i>Pathway</i>	<i>Site of Pain</i>
Uterus and Cervix	Distortion, stretching, tearing of fibres	Afferents which accompany sympathetic pathway to T10, T11, T12 and L1 Dorsal rami T10—L1 referred to cutaneous branches of posterior divisions	upper abdomen and groin' mid back
Periuterine Tissues & Lumbosacral region	Pressure often in association with fetal malposition or platypelloid pelvis	Lumbosacral plexus L5, S1 (? Pelvic splanchnic nerves)	low-back, thigh
Bladder ,Urethra, Rectum	Pressure by presenting part	S 2 ,3,4	referred to perineum and sacral area
Vagina	Distension, tearing	Somatic S2,3,4	Not referred
Perineum	Distension, tearing	Pudendal(S 2, 3, 4) Genitofemoral (L1, 2) Ileioinguinal L1 Posterior cutaneous Nerve of thigh, S2, 3	Not referred



MATERNAL AND FETAL CONSEQUENCES OF UNRELIEVED PAIN IN LABOUR

THE STRESS RESPONSE TO PAIN IN LABOUR

Segmental and supra-segmental reflex-responses from the pain of labour may affect respiratory, cardiovascular, gastro-intestinal, urinary and neuro-endocrine functions.

Respiratory - Pain in labour initiates hyperventilation leading to maternal hypocarbia, respiratory alkalosis and subsequent compensatory metabolic acidosis. The oxygen dissociation curve is shifted to the left and thus reduces tissue oxygen transfer, which is already compromised by the increased oxygen consumption associated with labour.

Cardiovascular - Labour results in a progressive increase in maternal cardiac output, primarily due to an increase in stroke volume, and, to a lesser extent, maternal heart rate. The greatest increase in cardiac output occurs immediately after delivery, from the increased venous return associated with relief of enocaval compression and the auto transfusion resulting from uterine involution.

Hormonal - Stimulation of pain results in the release of beta-endorphin and ACTH from the anterior pituitary. Associated anxiety also initiates further pituitary response. Pain also stimulates the increased release of both adrenaline and noradrenaline from the adrenal medulla which may lead to a progressive rise in peripheral resistance and cardiac output. Excessive, sympathetic activity may result in in coordinate uterine action, prolonged labour and abnormal fetal heart-rate patterns. Activation of the autonomic nervous system also delays gastric emptying and reduces intestinal peristalsis.

Metabolic - Maternal: During labour, glucagon, growth hormone, renin and ADH level increases while insulin and testosterone level decreases. Circulating free fatty acids and lactate also increase with a peak level at the time of delivery.

Fetal : Maternal catecholamines secreted as a result of labour pain may cause fetal acidosis due to low placental blood flow.

METHODS OF PAIN MEASUREMENT

As described earlier pain is a subjective feeling or experience that is influenced by factors like cultural learning , the situation, attention and other psychological variables .Most accepted version of pain is the three dimensional view of sensory-discriminative ,motivational-affective, cognitive-evaluative components.

Methods of pain assessment

1. Verbal numeric rating scale
2. Visual analog scale
3. McGill pain questionnaire
4. Descriptor – Differential scale

VISUAL ANALOG SCALE

Advantages:

- Widely used
- Simple, efficient, minimally intrusive measure of pain intensity.
- Exhibits ratio scale property
- Its conceptual simplicity provided that adequate clear instructions are given to the patients.

Disadvantages

- Pain is an uni-dimensinal experience when measured by it
- Bias of expectancy for change and reliance on memory

In this study VAS score of 0 indicates no pain and a VAS score of 100 indicated maximum pain.

METHODS OF LABOR PAIN RELIEF

There have been many approaches to the relief of pain in labour throughout history up to the present time. The requirements of satisfactory analgesic technique in labour may be listed as follows

1. Safety
2. Effective analgesia throughout painful periods of labour
3. No depressant effect on the maternal respiratory or cardiovascular system
4. No depressant effects on the progress of labour
5. No depressant effects on the baby before or after delivery
6. No unpleasant maternal side-effects
7. High technical success rate.

Unfortunately no one technique has all these properties

NON PHARMACOLOGICAL METHODS

Methods of psychological analgesia can be divided into three broad categories :

- Natural child birth - the Read method.
- Psychoprophylaxis - the Lamaze technique.
- Hypnosis

Each technique claims the elimination of pain without any harm to the mother, the baby or to the progress of labour and without the need for chemical analgesia. All require adequate antenatal preparation. Still most women experience severe labour pain. Furthermore, psychological analgesia can place increased demand on the staff.

Support during labour:

A friendly atmosphere in the labour room is preferable to help a woman to cope with pain. Homely surroundings help to allay anxiety and reduce the need for pharmacological analgesia.

TENS(trans cutaneous electrical nerve stimulation) (10)

TENS was introduced to relieve pain in childbirth in the early 1980s. Since then the use of TENS in labour has become increasingly popular as it is simple to use and is non-invasive. The mode of action depends on the two principal theories. One that A-fibres are stimulated by the electrical stimulation preventing the transmission of afferent noxious stimulus originating from C-fibres, the other that the electrical stimulus increases endorphins and enkephalins within the system. TENS electrodes are applied over the dermatomes supplied by T10 to L1. The TENS machine then gives a low background stimulus which can be augmented at the time of each contraction. It has been observed in clinical practice that TENS may provide limited pain relief during the first stage of labour. Meta-analysis of randomized controlled trials of TENS in labour does not, however, confirm its efficacy

SYSTEMIC

Opioids have been used for anaesthesia in labour for hundreds of years. However, it was not until the early twentieth century that techniques deliberately employing the analgesic effects of the opioids gained major attention. Unfortunately, dosage and effect are limited by maternal and neonatal side-effects, so that only moderate pain relief could be obtained with these drugs.eg..

Pethidine

Buprenorphine

Nalbuphine.

Tramadol.

Butorphanol

Fentanyl primarily acts on (MOP)mu-receptors and is approximately 80-100 times

potent as morphine. It has a rapid onset action and shorter duration of action. The peak analgesic effect occurs within 5 minutes and the duration of effect is about 30 minutes after 1 mcg/kg administered intravenously. Fentanyl is principally bound to albumin which favors its transplacental transfer. For analgesia in labour 50-100mcg/hour is required, given in increments of 10mcg IV.

REGIONAL

Lumbar epidural block

Caudal epidural block

Sub arachnoid block

Combined spinal-epidural

Lumbar sympathetic block

Paracervical block

Pudendal block

INHALATIONAL AGENTS

Several inhalational agents, both gaseous and volatile, have been used successfully in labour. The earliest to be used were ether, chloroform and cyclopropane, followed by trichloroethylene and methoxyflurane. Enflurane, isoflurane and desflurane are more recent additions. Analgesia during labour can be provided by the inhalational anaesthetic agents in subanaesthetic concentrations thus relieving pain whilst maintaining maternal consciousness and avoiding regurgitation or aspiration of stomach contents. In fact, the competence of the upper oesophageal sphincter is well maintained under light general anaesthesia, although lost under mild sedation with barbiturate or diazepam. Inhalational agents readily cross the placenta and the concentration in foetal blood soon approaches that of the mother but, since these agents are excreted almost entirely through the lungs, they are readily excreted from the newborn. The efficacy of inhalational analgesia depends on the analgesic strength of the agent and on how quickly it reaches analgesic concentration after the start of inspiration. A rapid offset with complete elimination between contractions would prevent accumulation completely.

Nitrous oxide is the best match in current use. Various portable machines exist for administration of nitrous oxide blended with oxygen through an on-demand valve.

Nitrous oxide concentrations can be varied from 0 to 75% in oxygen. For self-administration, a concentration above 50% nitrous oxide should not be allowed. Entonox, which is a mixture of 50% nitrous oxide and 50% oxygen is most commonly used. Nitrous oxide does not interfere with uterine activity (1)

Ether has several side effects including potent emetic effects with an unpleasant pungent odour, irritant to the respiratory tract and explosive. Chloroform has a pleasant odour, is non-irritant, more potent and faster acting than ether but has undesirable, dose-related side effects, namely arrhythmias and liver damage.

Methoxyflurane and trichloroethylene have been used for analgesia in

labour, but have been withdrawn for other, nonobstetric, reasons.

Enflurane and isoflurane have been given via a draw-over vaporiser in sub anaesthetic concentrations to relieve pain in labour. The usual concentrations, in oxygen, of enflurane and isoflurane for self administration are 0.3-1% and 0.2-0.7%.

Such concentrations will not change uterine contractility or responsiveness to oxytocin. The neonate is not affected by these analgesic concentrations of these inhalational agents. Enflurane, however, causes long- term drowsiness so was never popular. Both the agents are expensive and since neither shows a significant advantage over entonox in terms of analgesia they are unlikely to be widely used on their own.

Desflurane is the newest volatile agent to be applied in labour. The chief advantage of this agent is rapid onset and offset of action, however it is expensive and since it has not been shown to provide superior analgesia to entonox, it is unlikely to become a popular agent for labour analgesia

EPIDURAL SPACE-ANATOMY AND CHANGES IN PREGNANCY

The epidural space is the interval between periosteum lining the vertebral canal and the dura mater surrounding the canal in its extension from foramen magnum to lower end of dural sac

.Boundaries:

Superiorly : foramen magnum

Inferiorly : Sacro coccygeal membrane

Anteriorly : Posterior longitudinal ligament covering vertebral bodies and discs

Posteriorly : Anterior surfaces of laminae connecting Ligaments, roots of spines ligamentum flavum.

Laterally : pedicles and inter vertebral foramina

Contents:

- Dural sac
- Spinal nerve roots
- extra dural plexus of veins
- spinal arteries
- lymphatics and fat

Size:

Anterior portion - 1mm (through out the length)

posterolateral -at cervical leve 1.5-2mm

- at thoracic level 3-5mm

- at lumbar level 4-6mm

Changes in pregnancy

- the lumbar lordosis associated with pregnancy increases the technical difficulty in performing epidural or sub arachnoid puncture when midline method is carried out
- increased elastic tissue and softening of connective tissue and increased water content leads to difficulty in identification of epidural space by loss of resistance.
- Intermittent obstruction of IVC by enlarged uterus encourages venous drainage through alternate pathways and so the vertebral or azygos system dilate the epidural internal vertebral venous plexus which reduces the internal volume of the epidural space. Hence segmental doses are reduced in pregnancy.
- During contractions sudden efflux of blood from contracting uterus into the venous system increases the epidural pressure so the spread of anaesthetic solution in the epidural space will be exaggerated during a contraction so injection should not be made at this time. The risk of venous puncture by needle or catheter will be increased if either is inserted into the epidural space during contraction because of engorged vertebral plexus. In the non pregnant state the pressure in the lumbar epidural space is normally $-1\text{cm H}_2\text{O}$. In early labor between contractions pressure in the lateral position average $1.63\text{ cm H}_2\text{O}$ and raise to $4\text{-}10\text{cm H}_2\text{O}$ by the end of first stage of labor during contraction. Assuming the supine position will increase the epidural pressure further proportional to the degree of IVC obstruction so there is a positive pressure inside the epidural space in pregnancy. Hence methods for identifying the space which depend on the presence of negative pressure are not recommended.

ENTONOX

Entonox is the 50-50 mixture of nitrous oxide (N₂O) and Oxygen (O₂). It is a effective analgesic agent with rapid onset and offset characteristics. Due to the extensive experience in the use of Entonox and N₂O, its effects are predictable and reliable and it has proved to be a very safe agent with minimal side effects

HISTORY

Nitrous oxide was discovered and purified by Priestley, Mayow and Hales in the mid 1700's and in the late 1700's was used extensively due to its pleasurable effects. The American dentist Horace Wells first used it medically in 1844 to reduce the pain of tooth extraction. The first report of the use of nitrous oxide for the relief of labour pain appeared in 1880 in the *St Petersburg Medical Weekly*. In that publication, and in subsequent reports. Klikovich (or Klikowitsch) described his use of a mixture of 80% nitrous oxide and 20% oxygen in obstetric patients. During the late 1800's the use of N₂O became popular in the USA and was introduced into Europe, in 1867, by Quincy and Coulton. Interestingly, until the late 1800's nitrous oxide was used alone and without any supplemental air or oxygen, therefore some of the sedative and analgesic effects of the gas could have been due to hypoxia.

In 1881 N2O was introduced for pain relief in childbirth and in 1911 Guedel

described an analgesic technique (possibly the first patient controlled analgesia)

in which the patients self- administered a mixture of air and N2O during childbirth

and minor surgery.

BOC studied the N2O/O2 system after a suggestion from Tunstall in 1961 (8). It

was found that it was possible to store a homogeneous gas mixture containing up

THE ENTONOX ADMINISTRATION KIT





to about 75% N₂O at a pressure of 132 bar at ambient temperature, (pure N₂O liquefies at 50 bar at ambient temperature). Since the Introduction of Entonox into obstetric practice by Tunstall in 1961 and into the ambulance service by Baskett in 1970, Entonox has become the mainstay of analgesia for childbirth and pain relief in acute situations in many countries.

Today N₂O is an essential ingredient in anaesthesia. As Entonox, it is a vital part of analgesia for childbirth and is uniquely placed as an ideal agent for the treatment of short-term pain due to almost any cause

PROPERTIES

Nitrous oxide is a low-molecular-weight, odorless to sweet-smelling nonflammable gas of low potency and poor blood solubility. Although nitrous oxide is nonflammable, it will support combustion. Its poor blood solubility permits rapid achievement of an alveolar and brain partial pressure of the drug (see Fig.

1-17). The analgesic effect of nitrous oxide are prominent, but it causes minimal

SHOWING THE PIN INDEX SYSTEM OF 7



CYLINDER CONNECTED AND READY TO USE



Entonox is a gaseous analgesic agent that is composed of N₂O and O₂ in equal proportions. It is presented in cylinders that are painted blue with a white and blue shoulder.

Highest -5.5°C 117 bar

Cylinder -7°C 137 bar

Pipeline -30°C 4 bar

Storage

Entonox is stored in white or blue cylinders with blue and white shoulders with PIN INDEX of 7. It is supplied in cylinders at a pressure of 137 bar and must be stored above its pseudo critical temperature of -6°C. Below this temperature the N₂O liquefies in a process called lamination. If this occurs a high concentration of O₂ will be delivered first with little analgesic effect, but as the cylinder empties the mixture will become progressively more potent and hypoxic as it approaches 100% N₂O. If a cylinder has been exposed to cold below -6 degree C it should be warmed for 5 minutes in a 37 degree C water bath or for 2 hours in a room at 15 degree C. It should then be inverted three times before use.

When delivered via a pipeline at 4.1 bar the pseudocritical temperature is less than -30°C. In the large cylinders used for connection to a pipeline system via a manifold, gas is therefore drawn first from the bottom of the cylinder by a tube

Poynting effect

The Poynting effect involves the dissolution of gaseous O₂ when bubbled through liquid N₂O, with vaporisation of the liquid to form a gaseous O₂/N₂O mixture.

[Poynting, John Henry (1852-1914). English physicist, mathematician, and inventor.]

Pseudocritical temperature

The critical temperature of a gas is the maximum temperature at which compression can cause liquefaction. Mixing gases may change their critical temperature. The Poynting effect produces a 50:50 mixture which reduces the critical temperature of N₂O so Entonox has a pseudocritical temperature of -6°C.

The gas is contained at a pressure of 137 bar and is delivered to the patient by

using a pressure regulator and demand valve. The patient will self-administer the gas, under the supervision of an appropriate healthcare professional, by using a facemask or mouthpiece. Entonox is widely used as an analgesic agent but its mechanism of action has not yet been fully explained. It is known that the effects of Entonox take place within the pain centres of the brain and spinal cord and are related to the release of endogenous neurotransmitters such as opioid peptides and serotonin, and activation of certain opioid receptors. Also, Jevtovic-todorovic et al(9) found that N-methyl-D-aspartate (NMDA) receptor currents were inhibited by N₂O, and it is known that the NMDA receptor is involved in many CNS pathways that control sensations, such as pain and euphoria. Whilst many of the anaesthetic mechanism of N₂O remain unknown, there is increasing clarity as to the analgesic effects of this gas. A recent hypothesis suggests that Entonox has its analgesic effects by the activation of descending noradrenergic pathways due to release of opioid peptides in the peri-aqueductal grey area of the midbrain. These descending pathways are thought to modulate pain through the activation of alpha-2 adreno-receptors in the dorsal horn of the spinal cord.

Due to the physical properties of N₂O (namely its blood/gas solubility) Entonox works very quickly and analgesia is maximal within 2 minutes of inhaling the gas but its effects are apparent within a matter of breaths.

Recovery from the effects of N₂O is very rapid. Once inhalation of Entonox has stopped, there is fall of 35% in the arterial concentration within 30 seconds.

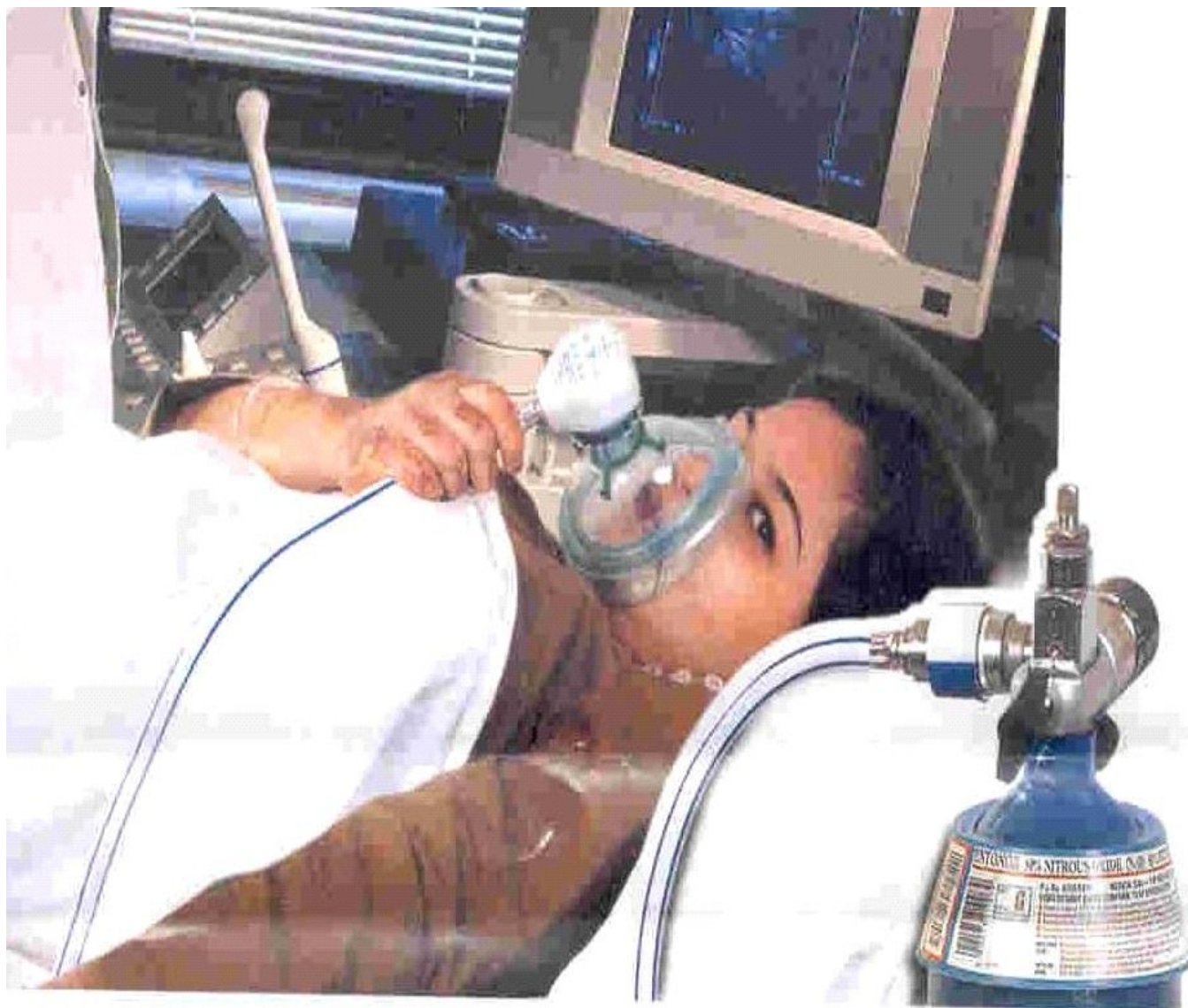
Studies have shown a subjective feeling of complete recovery, within 5 minutes, in individuals who breathed 40% N₂O for 30 minutes.

Although a relatively lipid insoluble inhalational agent, nitrous oxide needs to be inhaled for 45 seconds before the maximum analgesic effect can be obtained, so during the first stage, inhalation should be commenced at the first warning of a contraction and not delayed until pain appears. For optimum effect inhalation should start when the contraction tightens to co-ordinate the maximal effect with the central painful part of the contraction. Should unconsciousness occur, the patient drops the mask and recovery rapidly occurs. Once inhalation ceases, blood alveolar concentrations decline rapidly and the analgesic effect is very short lived. Pain dominates the whole of a second stage contraction and no warning is perceived by the mother. dependence should be placed on the

regularity of second stage contractions, and inhalation commenced at least 30 seconds before the next expected contraction. When the mother is bearing down late in the second stage she should quickly inhale 4 to 5 times from the machine, hold her breath and then push. The maneuver can be repeated if the analgesia wears off before the contraction is completed.

When used correctly, Entonox can be surprisingly effective. There are minimal cardiovascular, respiratory or neurological side effects. With the intermittent inhalation of nitrous oxide, nitrous oxide does not depress neonatal respiration or affect neonatal neurobehavior. (7) It should not be used in patients with a pneumothorax

SELF ADMINISTRATION OF ENTONOX BY A PATIENT



Due to the low fat solubility of N₂O, it does not accumulate to any great extent within the body and in addition N₂O is not metabolized by the body and will be eliminated completely by the lungs. (6)

The pharmacological profile of Entonox offers rapid onset of potent analgesia with speedy reversal of effects when required. This fast offset of action offers a clear advantage over all other analgesic agents, and if used in combination for pain relief allows a reduction in the doses of the other agents used (e.g. morphine, pethidine), thus reducing the often serious side effects associated with them.

Contraindications to Nitrous Oxide

N₂O should not be used for patients with bowel obstruction, pneumothorax, middle ear and sinus disease, and following cerebral air-contrast studies. Many anesthetists feel that use of N₂O should be restricted during the first two trimesters of pregnancy because of its effects on DNA production and the experimental and epidemiological evidence that N₂O causes undesirable reproductive outcomes. Since N₂O affects white blood cell production and function, it has been recommended that N₂O not be administered to immunosuppressed patients or to patients requiring multiple general anaesthetics.

Cardio-vascular system

Entonox has minor effects on the heart and circulation. In its use in general

anaesthesia, N2O is known to have a slight direct myocardial depressant effect

together with a weak stimulatory effect on the sympathetic system. The net effect is an unchanged or a very slightly decreased cardiac output, blood pressure and

systemic vascular resistance. The general opinion of the literature is that Entonox

has only a slight effect on cardio-vascular parameters and is safe in patients with

heart disease, even those who are hypovolaemic.

Respiratory system

The effect of Entonox on respiration are minimal. There is a small decrease in

tidal volume that is compensated for by a small increase in respiratory rate. The

combined effect of these changes is often a slight increase in minute ventilation

without a change in blood carbon dioxide (CO₂) levels.

Diffusion hypoxia is a phenomenon that can occur after inhaling N2O during

anaesthesia. It is due to N2O diffusing out of the body faster than nitrogen can

diffuse in, thus resulting in dilution of the O₂ contained within the lungs and a

reduction in arterial oxygen levels and saturation(5)

Gastro-intestinal system

The safety of Entonox in gastro-intestinal procedures has been shown. There were no significant alteration in bowel function

Nausea and vomiting

Nitrous oxide, when used in anaesthesia, may cause a weak emetic effect in certain individuals.

Enclosed gas spaces

The use of Entonox is contra-indicated in some cases where there is trapped air within the body, because N₂O will diffuse rapidly into the space, thus increasing its size.

The contra-indications include:

- Artificial, traumatic or spontaneous pneumothorax • Intestinal obstruction
- Air embolism • Decompression sickness • Head injuries with impaired consciousness • Myringoplasty • Recent underwater dive Intoxication • Following air encephalography • Maxillofacial injuries • Severe bullous emphysema
- Patient non-compliance

Effects on vitamin synthesis

The N2O component of Entonox can effect vitamin B12 synthesis by inhibiting the enzyme methionine synthetase. The effect may be of importance if the therapeutic exposure to Entonox exceeds 6-8 hours. If exposure of Entonox is greater than 6 hours N2O can also interfere with folate metabolism and DNA synthesis, which can impair bone marrow function But Nunn *et al* reported that evidence of actual harm to patients is lacking unless in extreme circumstances and stressed that the effects on vitamin B12 and folate require prolonged exposure.

Occupational exposure to Entonox (2) (3) (4)

Long term occupational exposure to significant levels of N2O can result in Myeloneuropathy — a condition similar to sub-acute combined degeneration of the spinal cord, in which there is peripheral sensory and motor impairment. This condition has been reported in individuals addicted to the inhalation of Entonox and N2O. There has also been concern that N2O exposure can lead to spontaneous abortion. This idea is based on work done on pregnant rats that were exposed to high levels of N2O for prolonged periods. There has been very little evidence that similar effects occur on humans, but a questionnaire by

Rowland *et al*¹⁵ suggested a slightly higher risk of abortion in dental nurses working in rooms without scavenging. Alternatively, a study involving almost 4000 midwives stated that the use of N2O/O2 is not associated with an increased risk of abortion. In order to reduce the risks to staff the Health and Safety committee has set an occupational exposure limit of 100 ppm over an 8-hour Period. This is a fifth of the dose at which no effects were seen in animal studies and represents a level at which there is no evidence that human health would be affected. A study by Henderson *et al* in 1999 showed that over a 14 month period, in the anaesthetic rooms, operating theatres and recovery rooms of 8 hospitals within Wales, the time weighted average levels all fell within the occupational exposure limit. The same standards apply to maternity units and dental practices where Entonox is used commonly, but these areas can often have raised exposure levels due to lack of effective ventilation and gas scavenging systems.

Environmental pollution

Nitrous oxide has little effect on the ozone layer, but does have a minor influence on the green house effect since it reduces heat radiation. However, the energy

information administration (USA) states the principle source of N₂O is the breakdown of fertilisers and natural compounds in the soil. Medical N₂O contributes only 0.5% of the total release of N₂O into the atmosphere in the USA. Nitrous oxide and Entonox have been used in pain relief, sedation and anaesthesia for more than 150 years. Millions, perhaps billions, of patients have been treated without any serious side effects or adverse events having been reported.

The effects of Entonox are fast. They are felt after only three or four breaths and are maximal after just 2 minutes. The effects also disappear rapidly once Entonox is removed and even with sensitive psychometric tests, it is difficult to display residual effects after 30-40 minutes.

Great strides have been made in the pre-hospital, emergency and hospital management of patients, yet the relief of pain and suffering is something that is often forgotten, or provided in a sub-optimal fashion. In addition, it is easy not to appreciate the pain the patient has or to overlook it as it is produced whilst one is seeking to help.

OPIATES

"God's Own Medicine"
Sir William Osler

Opioids refer to all exogenous substances natural and synthetic that binds specifically to any of the several sub population of opioid receptors. Opioid receptors were discovered by PERT and SNYDER in 1974

Mode of action of opioids

Opioid receptors are presynaptic. Activation of Gi proteins leads to inhibition by increased K⁺ conductance and hyperpolarisation of the cell membrane. The decrease in membrane excitability may decrease pre- and post-synaptic responses.

Opioid receptors

The existence of multiple opioid receptor subtypes arose from work identifying the different anatomical location and pharmacological profiles of compounds that were eventually used to name them:

- morphine (mu)
- ketocyclazocine (kappa)
- vas deferens (delta)
- A fourth opioid-like receptor has been included in the opioid receptor family and is termed the nociceptin orphanin FQ peptide receptor.

Sigma is not considered to be an opioid receptor, since responses induced by activation of this receptor are not reversed by naloxone.

International Union of Pharmacology (IUPHAR)

This body have declared that the new accepted nomenclature for opiod receptors is:

- MOP (mu)
- KOP (kappa)
- DOP (delta)
- NOP (nociceptin orphanin FQ peptide receptor)

Opioid receptor subtypes

MOP

The MOP receptor was the last of the classical opioid receptors to be cloned and is located throughout the central nervous system in areas involved in sensory and motor function including regions concerned with the integration and perception of these senses, for example the cerebral cortex and amygdala.

A high density of MOP receptors is found in the caudate putamen of the basal ganglia. MOP receptors are located pre-synaptically on primary afferent neurons within the dorsal horn of the spinal cord where they inhibit glutamate release and hence transmission of nociceptive stimuli from C and A-delta fibres. The periaqueductal grey (PAG) is an area of the midbrain involved in the central control of nociceptive transmission. Efferent outflow from the PAG descends to the spinal cord where it acts to inhibit nociceptive transmission in afferent fibres, this pathway is known as the descending inhibitory control pathway. High densities of MOP receptors are found in the PAG and the analgesia of some opioids may come about from removal of an inhibitory gamma-aminobutyric acid (GABA)-ergic tone in this region of the brain. GABA is the main inhibitory transmitter in the brain and acts to reduce or prevent antinociceptive outflow from the PAG.

Major side-effects associated with MOP agonists include respiratory depression through a reduction in the sensitivity of central and peripheral chemoreceptors to hypercapnia. MOP agonists further inhibit gastrointestinal tract secretions and peristalsis, often causing constipation. MOP opioids also have effects on the cardiovascular system, thermoregulation, hormone secretion and immune function.

DOP (Delta)

The DOP receptor was the first to be cloned and is less widely distributed relative to the other opioid receptors. The highest densities are found in the olfactory bulb, cerebral cortex, nucleus accumbens and the caudate putamen. DOP receptors are located pre-synaptically on

primary afferents where they inhibit the release of neurotransmitters.

Through both spinal and supraspinal sites, the receptor is involved in the antinociceptive/analgesic actions of some opioids. However, DOP receptor agonists have also been shown to reduce gastrointestinal tract motility and cause respiratory depression.

KOP (Kappa)

The kappa or KOP receptor was the second of the opioid receptor family to be cloned. The prototypical agonist of the kappa receptor is the non-peptide benzomorphan ketocyclazocine, the actions of which have been shown to be distinct from those elicited by stimulation of the MOP receptor, for example sedation without marked effects on heart rate.

NOP

At the cellular level, N/OFQ produces similar actions to those of the classical opioids resulting in reduced neuronal excitability and inhibition of transmitter release. However, exogenous administration has been shown to have effects on locomotion, stress and anxiety, feeding, learning and memory, reward/addiction and urogenital activity.

PHARMACOLOGY OF FENTANYL

FENTANYL CITRATE is a synthetic phenyl piperidine derivative MOP 2 receptor agonist

It is a chemical congener of reversed ester of pethidine

80-100 times as potent as morphine

Pharmacodynamics:

Respiratory system:

- Dose dependant respiratory depression through direct action on medullar respiratory centers.
- Apneic threshold increased
- Hypoxic drive reduced
- Chest wall rigidity-anti tussive action
- Delayed respiratory depression

Cardiovascular system:

- Bradycardia – due to central vagal stimulation in high doses
- No effect in cardiac contractility
- Hypotension especially in large doses due to bradycardia, venodilatation, suppression of central sympathetic outflow.

Central Nervous System

- Analgesia
- Euphoria
- Sedation/hypnosis
- Miosis
- Nausea /vomiting

GIT

- Delays gastric emptying
- Biliary spasm

Endocrine System

- Attenuation of stress response

Pharmacokinetics:

It has rapid onset of action less than 30 secs when given as a single intravenous dose

Highly lipid soluble and rapid redistribution

Lungs act as a large reservoir with 75% of the initial dose undergoing first pulmonary uptake.

Metabolism

Is by liver and undergoes N – dealkylation, hydroxylation, and amide hydrolysis to inactive metabolites namely norfentanyl and des propinyl nor fentanyl and excreted via bile

- Percentage bound to plasma proteins 84%
- $t_{1/2}$ 1-2 min

Epidural fentanyl

Clinical properties	Advantages	Disadvantages
Rapid onset	Rapid analgesia	Systemic absorption
Short duration	Decreased side effects	Brief single dose analgesia
Low CSF solubility	Ideal for continuous infusion	Minimal CSF spread

Since 1980 fentanyl is used for epidural analgesia

- Dose 50-200 mcg
- Onset 5-15 mins
- Duration 2-4 hours after single dose

When given intra-thecal these opioids should be injected as close as possible to the spinal segment where primary nociceptive afferent carrying the nociceptive impulse from involved dermatomes enter the spinal cord. When this is accomplished small dose of the drug will produce significant analgesia.

Effect On labor:

1. If given during the latent phase of the first stage of labor there is tendency for it to slow cervical dilatation and it may even result in uterine inertia.
2. Optimum dose has no significant depressant effect while an excessive dose delays labor.

Effect on fetus:

1. Direct effect after absorption depresses the fetus.
2. Indirect effect occurs if given in large doses through effects on maternal circulation and respiration

Side Effects:

- Pruritus
- Sedation
- Urinary retention
- Nausea
- Vomiting
- Apnea
- Seizures

Factors associated with respiratory depression:

- Poor general condition
- Elderly patients
- Hydrophilic opioids
- Concomitant use of other drugs

Over dosage:

- | | |
|--|---|
| 1. Apnea / Hypo-ventilation | Oxygen Administration
maintain airway
Endotracheal intubation
Assist respiration |
| 2. depressed respiration
With muscular rigidity | intra venous
neuromuscular
blocking agents required to
Assist or control respiration |
| 3. Hypotension | parenteral fluids |
| 4. Respiration depression | nalorphine, Levellorphan,
Naloxone |

PHARMACOLOGY OF BUPIVACAINE

It is an amide linked local anaesthetic. Synthesized by .A.F.Ekensham and introduced into clinical practice by Telivuo in 1963.

STRUCTURE

It is an amino amide local anaesthetic having aromatic moiety (benzene ring) which offers lipophilicity at one end of molecules linked by an amide to a tertiary amine which is hydrophilic on the other end of the molecule.

MOLECULAR FORMULA

It displays stereoisomerism; marketed as a racemic mixture containing optically active enantiomers R and S .S enantiomer has been noted to have a slightly longer duration of action yet lower systemic toxicity when compared to its R type.

MECHANISM OF ACTION:

The base form is in equilibrium, with the cationic form out side the axoplasmic membrane. The base form diffuse inside in the cell and then equilibrates with the cationic form which reaches the local anaesthetic receptor on the sodium channel by traversing channel pores while it is in the open state preventing sodium ions movement intracellular.

The second messengers system is also affected where the Adenylate cyclase and guanylate cyclase are involved and inhibition of synaptic transmission occurs. This may be due to presynaptic calcium channel blockade or post synaptic receptor modification

PHYSICOCHEMICAL CHARACTERISTICS

Molecular weight	288
Potency ratio	15
Toxicity ratio	10
pka	8.16
protein binding maternal	95
fetal	66
partition coefficient	346

PHARMACOKINETICS OF EPIDURAL BUPIVACAINE

The uptake of local anesthetics into blood vessels in the area where it has been deposited and its subsequent transfer into systemic circulation is generally defined to as systemic absorption.

Absorption

A biphasic absorption pattern has been found for epidural bupivacaine the rapid initial absorption following epidural administration is most likely related to high concentration gradient between drug on the solution and in the blood. Later on after the local anesthetic has been taken up into local tissues such as epidural fat absorption will become dependent on tissue blood partitioning resulting in slow absorption. With mean absorption time 8.6 hours. Bupivacaine will produce lower C MAX than less potent and less lipid soluble agents.

Distribution

Has some special emphasis on the pregnant patient, because one of the organs that will be exposed to absorbed drug is the fetoplacental unit.

Pharmacokinetics:

$T_{1/2}$	162 MIN
Vdss	73 lits
Clearance	.6 lit/min

Metabolism and elimination

Liver is a major site of metabolism. There are two major factors controlling the clearance of the amide-linked local anesthetic. They are hepatic blood flow and the blood function. The principal pathways of metabolism are N-Dealkylation. Aromatic hydroxylation and amide hydrolysis.

Factors affecting placental transfer of local anesthetics.

1. C Max
2. Utero-placental perfusion
3. Fetal disposition.
4. Feto-maternal ratio

Fetomaternal ratio refers to the amount of total drug that equilibrates between the fetus and the mother and includes the protein bound drug. The F/M ratio for bupivacaine is 0.3-4.4. However it is the unbound form that rapidly equilibrates across the placenta and with other compartment in the foetus. Hence if the maternal levels of drug are dangerously high, then the foetus will be exposed to similar concentration. For drugs that are highly protein bound such as bupivacaine the F/M ratio is of little clinical significance. The Half-life of bupivacaine in newborn is 8.1 hours and plasma protein binding is 66%. Bupivacaine appears to be safer in view of high protein binding, high PKA, and low F/M ratio.

CLINICAL CHARACTERSTICS

Penetrance	Moderate
Duration	6-8 Hrs
Infiltration	0.05 %
Field Block	0.1%
Pudendal/Para-cervical block	0.125%
Extra-dural Block	
For analgesia	0.125%-0.25%
For motor block	0.5%-0.75%
Toxic dose	2mg per Kg

Adverse effects and complications of local anesthetics

CNS toxicity

Potentially toxic blood level can occur if the drug is injected intra-venous and intra-arterially or if a large dose of drug is injected into a highly vascular area. Risk of CNS toxicity is more is because bupivacaine is highly protein bound drug. Pregnancy is associated with 30% reduction in protein binding which allows for higher brain levels of bupivacaine for a given dose of drug.

Symptoms

Slow speech, jerky movements, tremors, hallucinations, seizures.

Treatment

- Adequate ventilation with 100% oxygen
- Protection of airway
- Suppression of seizure activity (thiopentone 50-100mg/ midazolam 1-2 mg IV)
- Paralysis and endotracheal incubation

Cardio- vascular system

- Dose dependent, depression of contractility, dose dependant, depression of conduction in all conduction tissues.
- Progressive prolongation of ventricular conduction time.
- Predisposition to re-entry phenomenon followed by sudden onset of ventricular fibrillation.4 times more potent than lignocaine

Treatment

If cardio-vascular collapse occurs

- Start CPR
- Endotracheal intubation at the earliest
- Vigorous fluid resuscitation
- To improve venous return
 - Leg elevation
 - Left uterine displacement
 - Delivery of foetus
- Adrenaline
- Bretylium for tachyarrhythmias

REVIEW OF LITERATURE:

Harrison RF et al 1987

Conducted A comparative study of transcutaneous electrical nerve stimulation (TENS), entonox, pethidine + promazine and lumbar epidural for pain relief in labor. Analgesic effect, labor outcome, safety and patient satisfaction were compared in 170 primigravid women; 50 using TENS initially for pain relief, 20 using entonox, 50 pethidine + promazine and 50 lumbar epidural. 88% choosing epidural related it fully effective. 90% using entonox, 96% using TENS and 54% given pethidine + promazine found partial relief. 82% of patients given TENS and 80% given pethidine + promazine required additional analgesia. This was also needed by one of the 20 patients choosing entonox.

Women using entonox alone had the shortest labors and women using lumbar epidural, the longest. Operative delivery was significantly more common in women receiving lumbar epidural. No significant inter-group differences were noted in cord pH or Apgar scores. Parturients And midwives both gave high consumer satisfaction ratings to all methods--except for pethidine + promazine, whose use must therefore be questioned. The analgesic efficacy of lumbar epidural outweighs any possible side effects. Entonox appears suited to those able to cope with the earlier part of labor, drug-free.

Realization of the potential of TENS requires the design of machines specifically to cope with the quality of the labor.

Wang B et al 1994

Labor analgesia with nitrous oxide was studied in 34 parturients, and another 50 women taking no drug as the control group. The analgesic effect was satisfactory. By Mulleetr's pain in labor score, 91.18% women had score of 0-1, and their respiratory and circulatory functions were not affected. During inhalational analgesia the parturients remained conscious. Uterine contraction, progress of labor and neonatal Apgar score were not interferred, and postpartum bleeding was not increased. There was no complications in the treatment group. This study suggests that nitrous oxide with enough oxygen inhalation is one of the good drug for obstetric analgesia, but its concentration must be strictly controlled.

Su F et al 2002

A total of 1300 cases of term primiparous women in labor were divided into two groups. Study group (n = 658) 50% nitrous oxide in oxygen was inhaled during labor for relieving labor pain. Control group (n = 642) intermittent inhalation of 50% oxygen was carried out during labor. Two groups were compared with following indices: duration of the labor, delivery mode, meconium stained of amniotic fluid, postpartum bleeding volume, neonatal Apgar score, side effect of nitrous oxide, and blood gas analysis of samples from maternal radius artery and fetal umbilical blood. RESULTS: The efficiency of relieving labor pain in study group was much better than that of control group (80.9% vs 0.9%, $P < 0.001$). Rate of cesarean section in study group was lower than control group (11.6% vs 19.3%, $P < 0.05$). The active phase of labor in study group was shorter than control group (153 min vs 187 min, $P < 0.05$). There was side effect of dizziness in 39.4% cases of study group but there were no any complaint in the control group cases. There were no significantly differences in duration of the labor, meconium stained amniotic fluid, postpartum bleeding volume, neonatal Apgar score, and blood gas analysis between two groups ($P > 0.05$). CONCLUSION: Inhalation of 50% nitrous oxide in oxygen was safe and effective labor analgesia. It is acceptable. The measure of relieving labor pain may increase the vaginal birth rate. There is no severe side effect on mother and baby.

Ou X et al 2001

A total of 100 cases of pregnant women were provided with nitrous oxide premixed with oxygen (50%:50%) (control group); Another 100 cases were provided only with oxygen (comparison group). Recording duration of the Labor, way of delivery, bleeding volume, Apgars score, blood gas analysis to maternal radius artery and fetal umbilical blood among all patients. RESULTS: The effect for analgesia labor of the premixed gas was much better than that of control group, but there were no significant differences in time of labor, bleeding volume, Apgars score between the two groups. CONCLUSIONS: The inhalation of nitrous oxide premixed with oxygen (50%:50%) for analgesia labor benefits pregnant women because of keeping them being a good mental and physical condition. The inhalation of nitrous oxide for analgesia labor is a safe, effective and easy method.

Hart EM et al 2003

Conducted a retrospective analysis of the obstetric effects of introducing a low-dose epidural regimen for epidural analgesia in labour. Before this, all women in this unit requesting epidural analgesia for labour received intermittent boluses (10mL) of 0.25% bupivacaine. After the introduction of the low-dose service in March 2000, intermittent boluses (10mL) of 0.1% bupivacaine with fentanyl 2 micrograms per ml were given. The groups were compared for outcome of labour, quality of analgesia and any adverse events related to the epidural analgesia. There was a significant reduction in the low-dose group in the number of women requiring instrumental delivery 41% vs. 29% The need for indwelling bladder catheters was also reduced in the patients receiving the low-dose regimen 21.3% vs. 4.7%,. Duration of analgesia was longer in patients receiving bupivacaine 0.25% (mean minimum time between The need for further anaesthetic intervention was higher with the low-dose regimen 24% vs. 4% Maternal satisfaction was high in both groups (95 and 97%, respectively). We conclude that the introduction of a low-dose regimen of epidural analgesia for labour reduces the incidence of instrumental deliveries. It also decreases the incidence of bladder catheterisation during labour,

Jevtovic-todorovic et al

Found that N-methyl-D-aspartate (NMDA) receptor currents were inhibited by N2O, and it is known that the NMDA receptor is involved in many CNS pathways that control sensations, such as pain and euphoria. While many of the anaesthetic mechanism of N2O remain unknown, there is increasing clarity as to the analgesic effects of this gas

Stewart et al 1983

Showed the safety of Entonox in pre-hospital care in a 1983 study of over 1000 patients. They found no serious complications, but reported the following minor side effects:

- 10.3% dizziness
- 3.7% excitement
- 5.7% nausea
- 0.3% numbness

7.6% became drowsy or fell into a light sleep but all could be readily roused by verbal command, all could cough and swallow on request and no cardiovascular side effects were noted.

Nicola S. Wallace et al 2003

Parturients are nowadays encouraged to document their wishes for labor and delivery, including those for analgesia, in a birth plan. Informed consent is necessary prior to epidural insertion, but is difficult to obtain from a parturient in severe pain, who may already have received Entonox or opioid analgesia.

A retrospective survey of 100 random postnatal women. Parturients were interviewed at 24 – 72 hrs post partum regarding their antenatal wishes for labor analgesia, reasons for this choice, the actual analgesia received, what type of analgesia they would wish for future labors, what they would advise their friends to use, and their generalised satisfaction. Medical notes were examined for a previously documented birth plan and the labor partogram. Results: In the antenatal period, 80% of all women had documented a birth plan for labor analgesia. Both pharmacological and non pharmacological methods of analgesia were cited. For nulliparous patients, the most common reason for antenatal choice of labour analgesia was because of friends' rather than professional advice. Whilst 28% had planned epidural analgesia, 72% actually received it. Most parous women planned to use what they had received in a previous labour for analgesia. 44% planned whilst 48% received epidural analgesia. For nulliparous women there was a significant increase in analgesia requirements from that planned ($p = 0.039$). Parous patients tended to have decreased requirements from that planned. 86% of women who changed their mind to request epidural analgesia despite no advance planning, did so because they experienced greater pain than they had anticipated

prenatally. No patient was unhappy that she had received epidural analgesia when she had not actively planned this. 98% of those who had received epidural analgesia said that they would request this in subsequent labours, compared with 76% of those who had used Entonox only and 68% of those who had received Pethidine. The majority would also advise their friends to use epidural analgesia.

Conclusions:

1. Most women in labor want epidural analgesia.
2. Women in labor, especially nulliparas, will change their minds.
3. Birth plans for labor analgesia are therefore not predictive.
4. Anesthesiologists should be flexible.
5. Friends are more influential than prenatal classes.
6. Maternal satisfaction with epidural analgesia in labor means that the anesthesiology workload in labor ward will increase.

MATERIALS AND METHODS

The Current study was conducted in the Govt. RSRM lying in hospital. Chennai. Forty healthy primi parturients aged between 19-25 years were selected for study. The selection was purposive and patients with ASA class 1 physical status were taken up.

Institutional approval was obtained..

A prospective randomized trial was conducted. Randomization was done by Third party selection marked slips for each patient.

Inclusion criterion;

Primipara

Age 18 to 28 years

Weight 45 to 60 kgs

Height 145 to 165 cms

ASA class I

Cervical dilation 3 - 5 cms

Effacement > 50 percent

Willingness for Epidural

Willingness for Entonox

Able to understand usage of Entonox

Exclusion Criterion

Patient refusal

Multipara

Age, Weight, height parameters outside the range in the inclusion criterion

Any co- morbid condition (Diabetes, PIH, Cardiac disease etc)

Any obstetric complications

Any of the exclusion criterion for Entonox

METHODOLOGY

The patients were counseled at the beginning of the procedure about the Technique for which they were randomized. This was to gain the trust of the patients and as for Entonox the correct technique for using it was taught to the patient.

Here some patients who could not understand the correct usage either due to language problem were excluded from the study. Consent was obtained, complications explained and a brief physical status examination was done .all baseline parameters like Heart rate, respiratory rate, Systolic and Diastolic Blood Pressure, FHR, SPO2, Baseline VAS, were evaluated and recorded.

The patients were explained in detail about the visual analogue score and its usage. All doubts were cleared and a baseline VAS was recorded.

ENTONOX GROUP

The patients remained in the labour ward itself. A >15 degree wedge was placed under the Right hip. A tablet of Ranitidine 150 mg PO and a Metoclopramide 10 mg PO with small sips of water were given (33). All emergency drugs, equipment were checked and kept ready.

All the staff including Obstetricians, Paediatricians, staff nurses and workers were familiarized with the technique both as a way of enlisting their help and to teach them.

Cervical dilation and effacement was measured and if satisfactory the kit given to the patient and asked to use as explained to her. The patients were asked to take deep breaths of the gas and exhale slowly. They were asked to start using the gas as soon they perceive a contraction and not when they feel pain and continue till the end of contraction. This way when they have maximum pain at the peak of contraction they are already under the effect of Entonox. To obtain good pain relief the analgesic concentration of N₂O in the blood and thus the brain at the peak of contraction must be there.

Safety of the intermittent technique depends on the patient using and controlling the breathing system without assistance. Inhalation of Entonox from the standard breathing system is only possible if the patient opens the demand valve attached to the cylinder by creating a negative pressure. Creation of the negative pressure is only possible if the facemask is firmly applied to the face, producing an air-tight seal.

If the patient's level of consciousness is depressed she will be unable to maintain the seal, administration of Entonox will cease and the patient will begin to breathe room air. Full consciousness will return rapidly (Any attempt by the husband, nurse or doctor to 'help' the mother hold the mask in place will override this safety feature. The patient may then be anaesthetized and -may regurgitate gastric contents while her airway is unprotected.

SPO2 and pulse rate were monitored throughout using a pulse oxymeter. Progress of labour and FHR were assessed and recorded by the obstetrician Blood pressure and respiratory rate were recorded at regular intervals. The occurrence of side effects and complications were noted.

EPIDURAL GROUP

After the patient accepted epidural analgesia for pain relief, A preanesthetic evaluation was performed, which included an assessment of the patient's medical and anesthetic history. The risks of epidural analgesia are discussed with the patient, and informed consent was obtained The obstetrician was consulted to confirm the following That the patient is in labor and the obstetrician is committed to delivering the infant; and that all relevant obstetric issues are understood (e.g., gestational age, intrauterine growth restriction, fetal presentation, risk of obstetric hemorrhage, previous cesarean delivery). An assessment of fetal well-being is performed in consultation with the obstetrician

The necessary monitors, boyles machine, the emergency drugs and resuscitative kit were checked and kept ready in case of necessity.

ADMINISTRATION OF EPIDURAL ANALGESIA FOR LABOR: THE TECHNIQUE

1. Informed consent was obtained, and the obstetrician was consulted.

2. Monitoring included the following:

Blood pressure every 1 to 2 minutes for 15 minutes after giving a bolus of local anesthetic;

Continuous maternal heart rate monitoring during administration of Epidural.

Continual verbal communication.

3. The patient was hydrated with 500 mL of Ringer's lactate solution. (19.a) (19.b)
(20) (21)

4. The patient assumed a sitting position . Under strict aseptic precaution EPIDURAL proceeded with the patient. (22)

5. 17-gauge Tuohy needle used and introduced through the L3-L4 inter space The epidural space was identified with a loss-of-resistance technique.

6. The epidural catheter (multi orifice) was threaded 4 to 6 cm into the epidural space.

7. A test dose of 3 mL of 0.25% bupivacaine with 1:200,000 epinephrine was injected after careful aspiration and after a uterine contraction (to minimize the chance of confusing tachycardia that results from pain with tachycardia as a result of intravenous injection of the test dose). (18)

8. If the test dose was negative, 10mL of 0.125% bupivacaine with 2 micrograms per ml fentanyl was injected to achieve a cephalad sensory level of approximately T10.' Assessments were made every 2 mins for the first 10 mins and every 5 mins till 30 mins and then every 30 mins till next top up (24)

9. The patient is cared for in the lateral or semi lateral position to avoid aortocaval compression (23) HR, BP, SPO2, FHR was monitored. VAS scale assessed at peak of each contraction and the time of the establishment of epidural blockade was identified by loss of pinprick sensation and this time was noted. VAS scoring was

performed at timed intervals after each top up till the end of delivery. Vitals monitored and hypotension defined as a decrease of 20% from the base line was treated with ephedrine. Sensory level was noted after each top up.

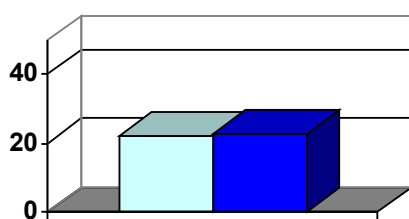
Progress of labor was assessed hourly by the obstetrician. The occurrence of side effects or complications was noted. This was followed by top up doses of 5 ml of the study solution was given on an hourly basis irrespective of the pain status. If the second stage started after 30 min of the preceding dose then 5 ml was injected in the sitting position. If it was less than 30 min then top up was not given and the vas score was assessed after 10 min. If the patient did not receive adequate pain relief within 30 mins then an additional 5ml of the study solution was given and the top up doses were administered 1 hour from then.

Mode of delivery noted and if other than normal the reasons for the intervention noted.

Duration of 1st stage of labor – time from when patient is handed over to us after noting the cervical dilation (Cervical dilatation >3cms Effacement >50%) to the full dilation of cervix noted.

Duration of 2nd stage noted

AGE IN YEARS

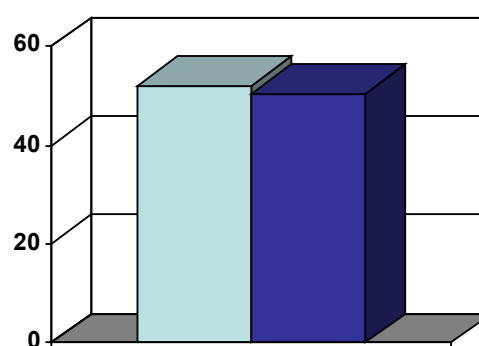


EPIDURAL	22.3
ENTONOX	22.7

EPIDURAL ENTONOX

**SD Epidural Group
COMPARISON OF MEAN AGES
USING UNPAIRED T TEST
P VALUE 0.4705
CONSIDERED NOT SIGNIFICANT
THEY ARE HENCE COMPARABLE**

WEIGHT IN KGS

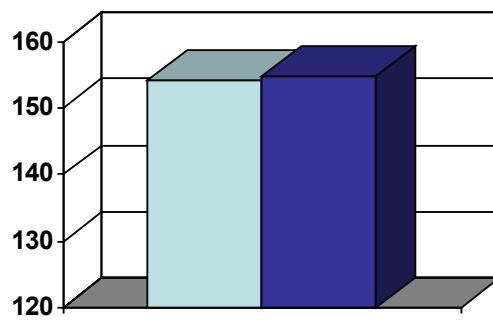


EPIDURAL	52.15
ENTONOX	50.6

EPIDURAL ENTONOX

**COMPARISON OF MEAN WEIGHTS
USING UNPAIRED T TEST
P VALUE IS 0.2409
NOT CONSIDERED SIGNIFICANT
THEY ARE HENCE COMPARABLE**

HEIGHT IN CMS

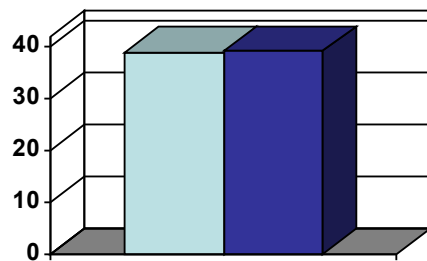


EPIDURAL	154.25
ENTONOX	154.95

EPIDURAL ENTONOX

COMPARISON OF MEAN HEIGHT
USING UNPAIRED T TEST
P VALUE IS 0.6303
NOT CONSIDERED SIGNIFICANT
THEY ARE HENCE COMPARABLE

GESTATIONAL AGE IN WEEKS

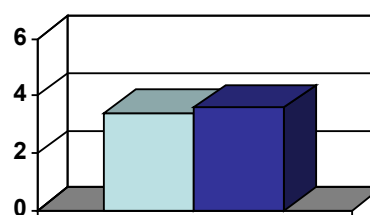


EPIDURAL	38.75
ENTONOX	39.1

EPIDURAL ENTONOX

COMPARISON OF MEAN GESTATIONAL AGE
USING UNPAIRED T TEST
P VALUE IS 0.1851
NOT CONSIDERED SIGNIFICANT
THEY ARE HENCE COMPARABLE

CERVICAL DILATION WHEN ANALGESIA ADMINISTERED (IN CMS)

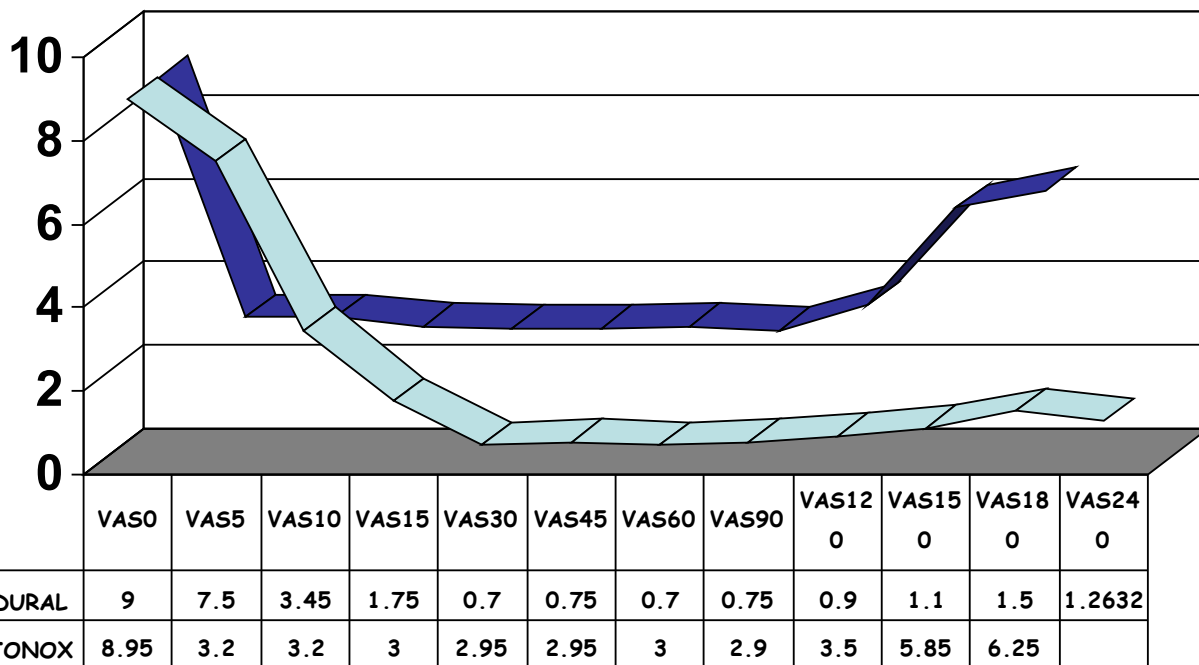


EPIDURAL	3.4
ENTONOX	3.6

EPIDURAL ENTONOX

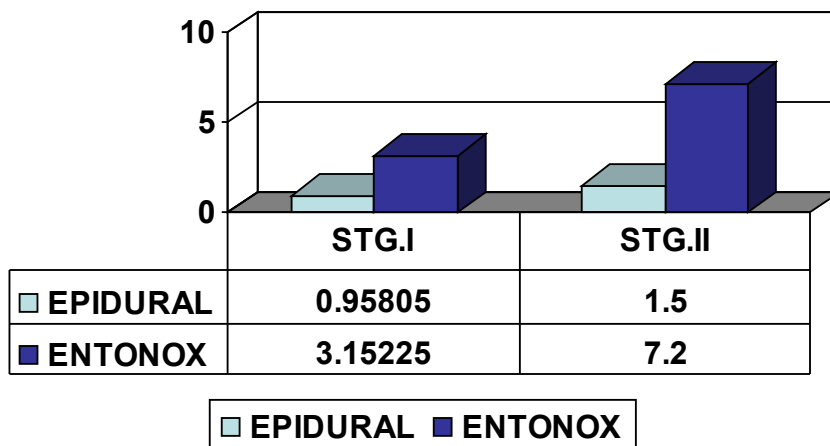
COMPARISON OF MEAN CERVICAL DILATION
USING UNPAIRED T TEST
P VALUE IS 0.3841
NOT CONSIDERED SIGNIFICANT
THEY ARE HENCE COMPARABLE

VAS



EPIDURAL ENTONOX

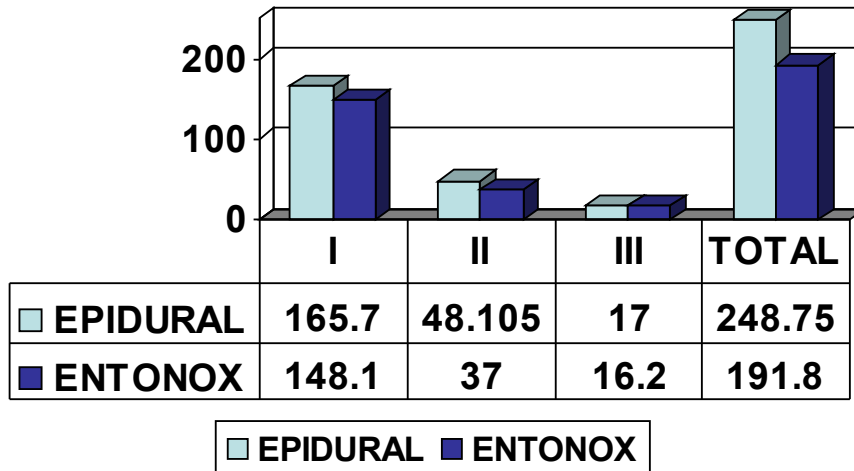
AVERAGE VAS



STAGE I
STAGE II

Using Mann Whitney U test
P VALUE IS 0.0001 CONSIDERED SIGNIFICANT
P VALUE IS 0.0001 CONSIDERED SIGNIFICANT

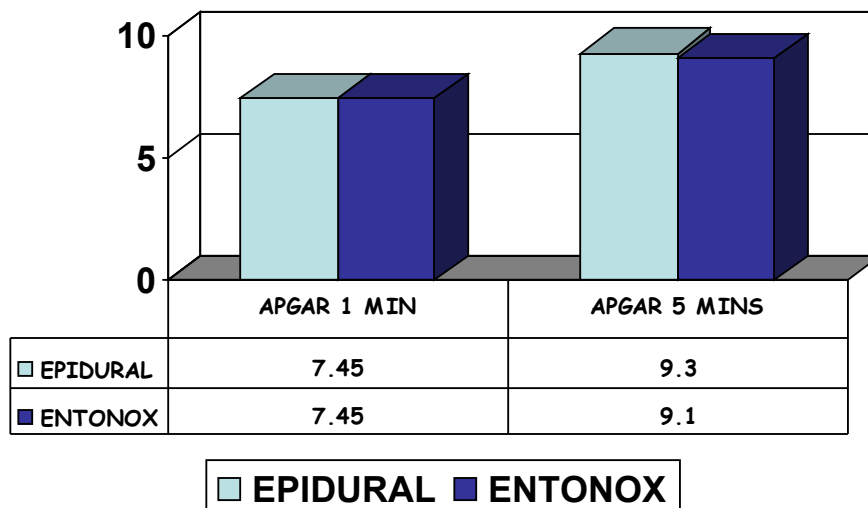
DURATION OF LABOUR IN MINUTES



Using unpaired t test
 STAGE I P VALUE IS 0.0001 CONSIDERED SIGNIFICANT
 STAGE II P VALUE IS 0.0001 CONSIDERED SIGNIFICANT
 TOTAL DURATION P VALUE IS 0.0001 CONSIDERED SIGNIFICANT

IN EPIDURAL GROUP THE DURATION OF BOTH THE FIRST STAGE AND SECOND STAGES ARE PROLONGED.

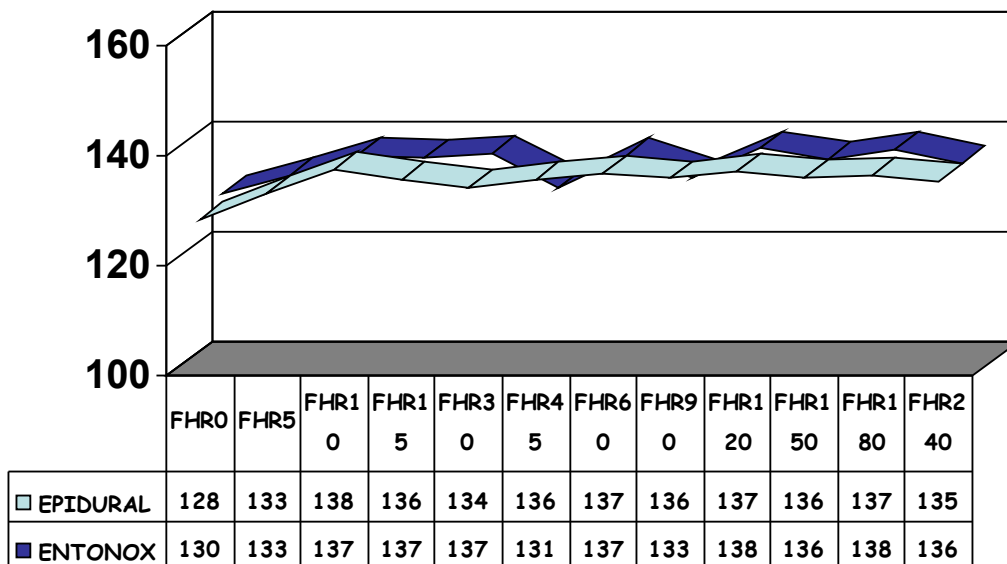
APGAR



COMPARISON OF AVERAGE APGAR SCORES

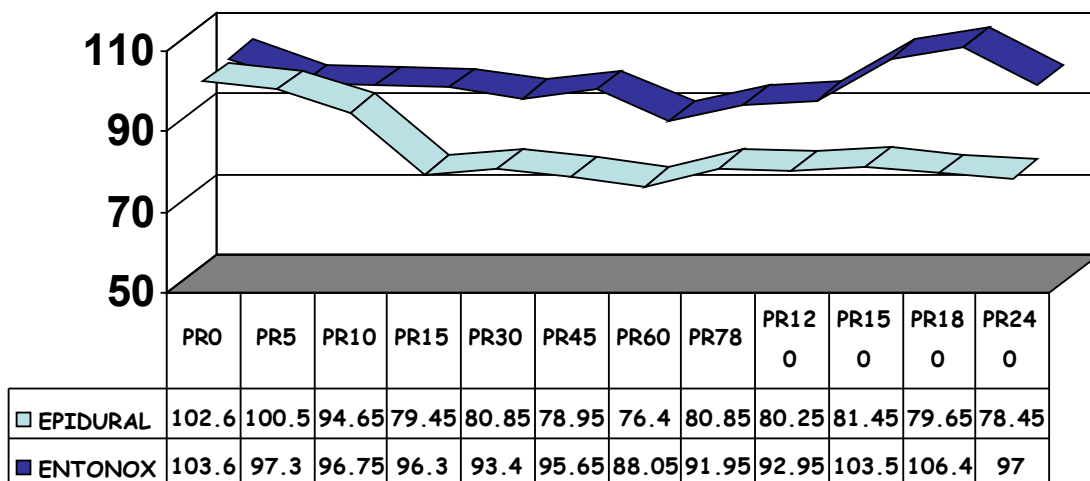
Using Mann Whitney U test
 APGAR 1 MIN p VALUE IS 0.3823 NOT CONSIDERED SIGNIFICANT
 APGAR 5 MIN p VALUE IS 0.1378 NOT CONSIDERED SIGNIFICANT

FHR



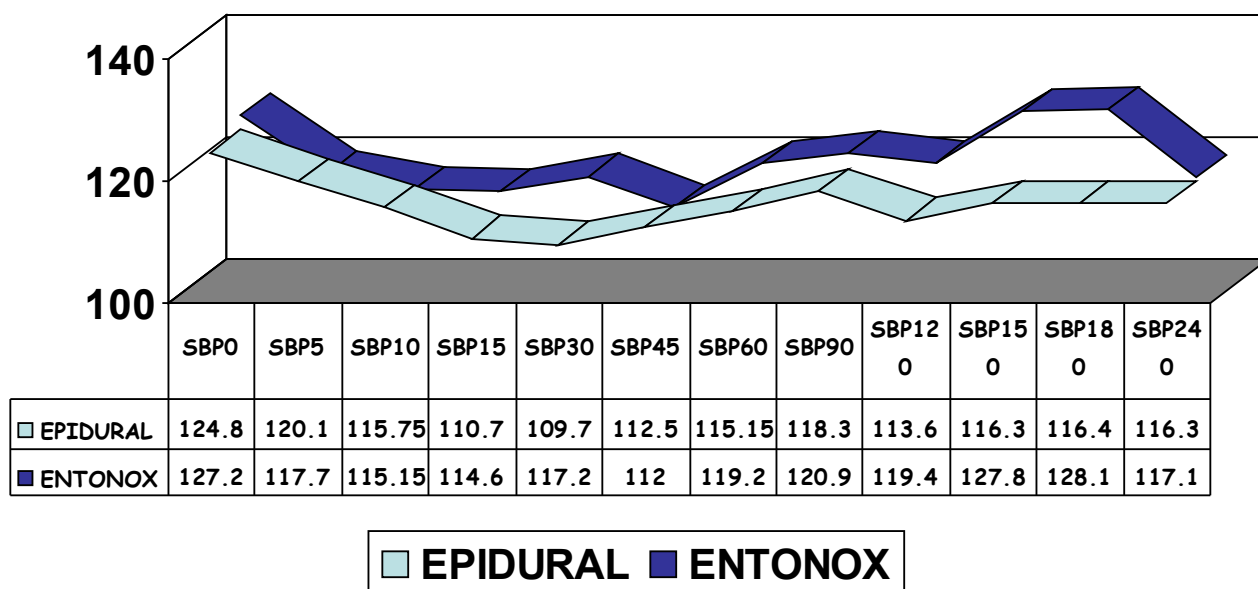
EPIDURAL ENTONOX

PULSE RATE

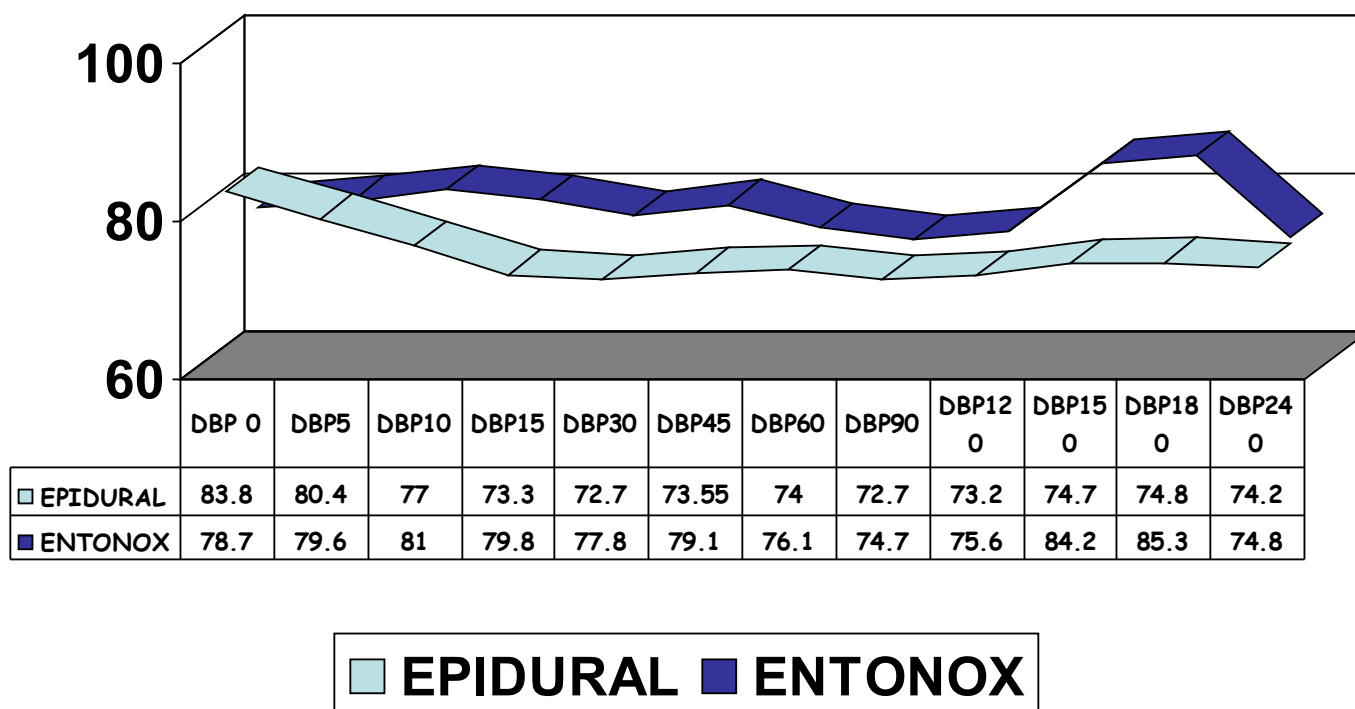


EPIDURAL ENTONOX

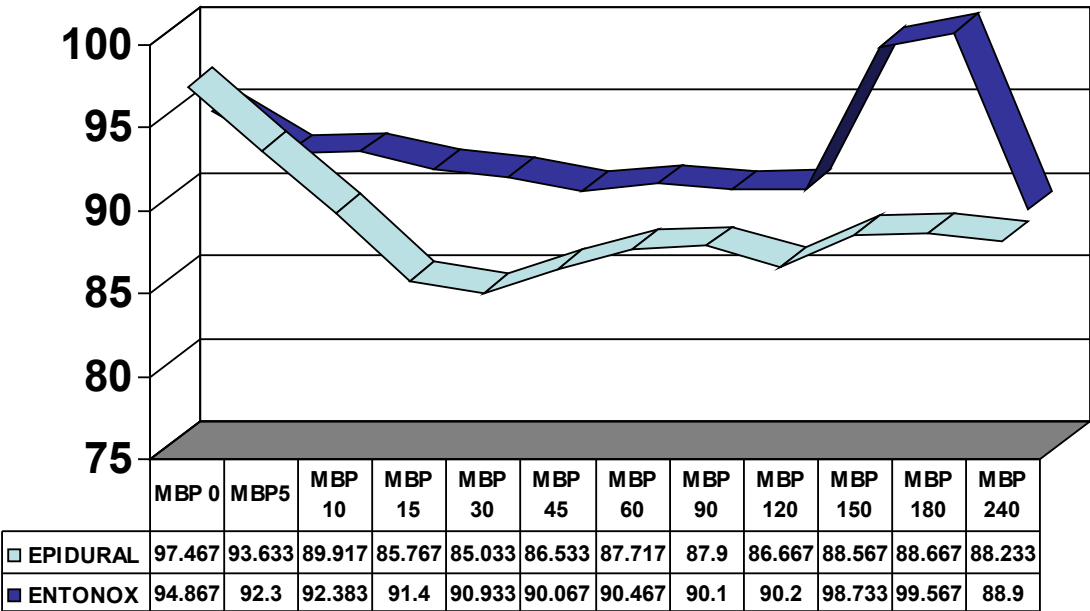
SYSTOLIC BLOOD PRESSURE



DIASTOLIC BLOOD PRESSURE

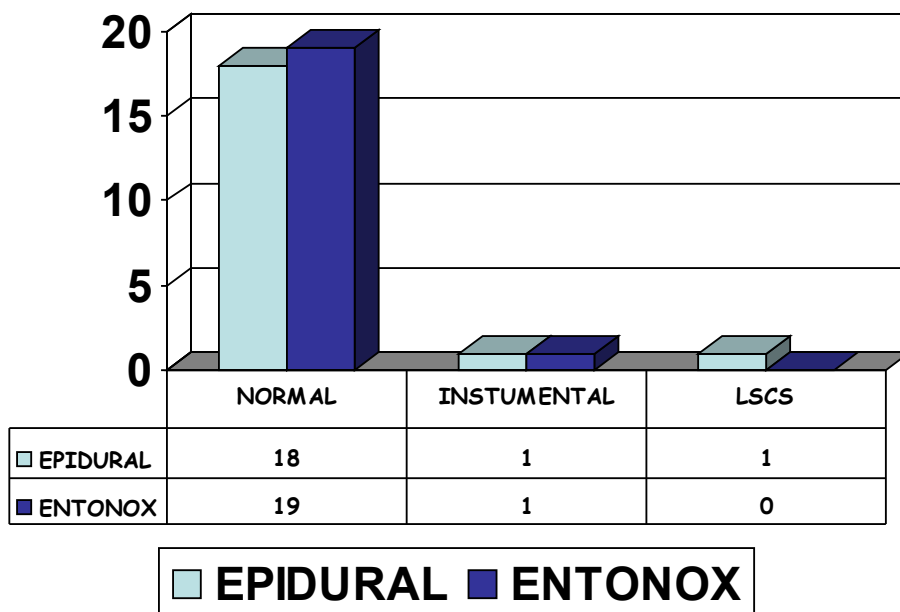


MEAN BLOOD PRESSURE



EPIDURAL ENTONOX

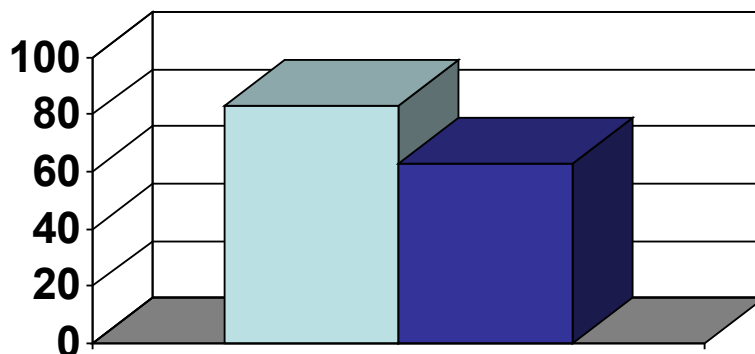
TYPE OF DELIVERY



MATERNAL SIDE EFFECTS

Side effects	EPIDURAL	ENTONOX
Dural puncture	0	-
Venous puncture	0	-
Pruritus	2	1
Nausea/vomiting	1	4
Rigor	2	0
Sedation	0	17
Hypotension	0	0
Urinary retention	7	0
Resp depression	0	0
Dry mouth	0	8

PT. SATISFACTION IN RUPEES



EPIDURAL	83
ENTONOX	63

EPIDURAL ENTONOX

COMPARISON OF MEAN PATIENT SATISFACTION

p VALUE <0.0001

CONSIDERED SIGNIFICANT

SUMMARY OF OBSERVATIONS

	EPIDURAL	ENTONOX
AGE (IN YEARS)	22.8 \pm 1.83	22.7 \pm 1.625
WEIGHT (IN KGS)	52.15 \pm 3.375999	50.6 \pm 4.739531
HEIGHT (IN CMS)	154.25 \pm 4.24109	154.95 \pm 4.860962
GESTATIONAL AGE (IN WEEKS)	38.75 \pm 0.786398	39.1 \pm 0.852242
CERICAL DILATION (IN CMS)	3.4 \pm 0.680557	3.6 \pm 0.753937
VAS SCORE I STAGE	0.95805 \pm 0.245036	3.15225 \pm 0.429585
VAS SCORE II STAGE	1.5 \pm 0.492592	7.2 \pm 0.695852
DURATION OF LABOUR I STAGE (IN MINS)	165.7 \pm 11.7029	148.1 \pm 11.7065
DURATION OF LABOUR II STAGE (IN MINS)	46.5 \pm 7.324955	37 \pm 6.496963
TOTAL DURATION OF LABOUR (IN MINS)	248.75 \pm 15.74894	191.8 \pm 17.22788
PATIENT SATISFACTION (IN RUPEES)	83 \pm 8.645047	63 \pm 16.88974

DISCUSSION

There exist a number of methods to provide pain relief in the laboring patient from psychological to the advanced regional techniques like combined spinal epidurals.

This study sets out to compare the Entonox inhalational technique with a Technique that is considered a gold standard for labour analgesia namely Epidural technique.

In this study the concentration of the local anaesthetic was 0.125 percent with 2 ug/ml Fentanyl as this low concentration provides very minimal motor blockade.

Blayert et al demonstrated minimal motor blockade with the use of 0.125 percent Bupivacaine in his study and confirmed by studies by Meister et al and Dresner et al.

Since there is a synergy between epidural opioid and local anaesthetic solutions reflecting separate sites of action namely opioid receptors and neuronal axons respectively. So, when these two are combined very low concentrations of local anaesthetic and Opioids can be used and avoid these side effects of hypotension and drug toxicity- Morgan Clinical Anaesthesiology III Edition Pg 826-827.

Effectiveness of Pain relief:

I stage:

The average VAS score for The Epidural Group was 0.958 and for the Entonox group was 3.152.

II Stage:

The average VAS score for The Epidural Group was 1.5 and for the Entonox group was 7.2. Though the patients had lesser pain relief in the Entonox group in the II stage when compared to the first stage it must be remembered that the II stage occupies a very small duration of the total labour and reasonable pain relief in the I stage is good for the patient. Moreover for the patients the II stage passes off in a blur... The patients are distracted by the efforts to bear down, by the constant entreaties by the attending staff to bear down and the thrill of seeing the baby emerge. This constant activity in many ways distracts the patient from

the pain.

Average time for the Patient to Experience pain relief in Entonox Group : 44.7 seconds

Overall Patient Satisfaction:

The Epidural group patients said that they will give an average score of 83 rupees for satisfaction and the Entonox group said that they will give 63 rupees.

Harrison RF 1987 (26)

88% choosing epidural related it fully effective while 90% using Entonox found partial relief. Entonox appears suited to those able to cope with the earlier part of labor, drug-free.

Rosen MA 2002(27)

Showed that A systematic review of 11 RCTs comparing Entonox with placebo or other inhaled agents showed that Entonox provided a consistent but moderate analgesic effect

Benhamou D Et al 2002 (28)

State that Epidural analgesia is the most efficient technique for labor pain relief

Su F Et al 2002 (29)

State that: The efficiency of relieving labor pain in study group (Entonox) was much better than that of control group (50% O₂)

Duration of labour:

I stage

The mean duration in The Epidural group was 165.7 minutes and in the Entonox group was 148.1 minutes.

II stage

The mean duration in The Epidural group was 48.1 minutes and in the Entonox group was 37 minutes

Overall duration:

The mean duration in The Epidural group was 248.75 minutes and in the Entonox group was 191.8 minutes

Chestnut Obstetric Anaesthesia Pg 369

States:Epidural analgesia during labour is associated with increased risk of prolonged labour.

Kilpatrick and Laros 1989 (30)

Concluded that the use of regional anesthesia significantly prolonged the first and second stages of labor in both nulliparous and parous women

Thorp et al 1993 (14)

In their study :Randomized 93 nulliparous women to receive either epidural Bupivacaine or intravenous meperidine analgesia. The mean \pm standard deviation (SD) duration of the first stage of labor was 676 ± 394 minutes in the epidural group versus 519 ± 279 minutes in the meperidine group ($P < 0.05$).

Sharma et al 2002 (31)

State that :Active phase of I stage was 1 hour longer in the epidural group when compared to the meperidine group

Fetal Outcome

The Apgar scores:

1 minute:

The average score for the Epidural group was 7.45 and for the Entonox group was 7.45

5 minutes

The average score for the Epidural group was 9.25 and for the Entonox group was 8.9.

The fetal outcomes of both the groups were comparable and differences not significant. All the babies in both the groups were well and healthy.

Su F Et al 2002 (29)

Say that :There were no significantly differences neonatal Apgar score between study group (Entonox) and that of control group (50% O₂) .Inhalation of 50% nitrous oxide in oxygen was safe .There is no severe side effect on mother and baby

Harrison RF et al 1987 (26)

Did A comparative study of transcutaneous electrical nerve stimulation (TENS), entonox, pethidine + promazine and lumbar epidural for pain relief in labor No significant inter-group differences were noted in cord pH or Apgar scores.

Stefani SJ 1982 (7)

Concluded that neither enflurane nor nitrous oxide analgesia adversely affects neonatal neurobehavioral status at 15 min, 2 h, or 24 h of age. In their study Neonatal neurobehavioral effects of inhalation analgesia for vaginal delivery.

Oxygen saturation:

No patients in both Epidural group or Entonox group had SPO2 less than 95 % in any part of labour.

Su F 2002 (29)

State that : There were no significant differences in the blood gas analysis between two groups(study group (Entonox) and that of control group (50% O2))

Carstoniu J et al 1994 (32)

Intermittent self-administered 50% nitrous oxide in oxygen does not appear to predispose parturient women to hemoglobin oxygen desaturation

Mode of delivery

1 patient in Epidural group and 1 patient in Entonox group were delivered by using outlet forceps. The indication was maternal exhaustion. The babies were found to have cord around neck .1 patient in the epidural group was delivered by LSCS .

Hemodynamic parameters like Pulse rate ,Systolic and Diastolic pressures and Respiratory rate were relatively more in the Entonox group than in the Epidural group and even more so in the second stage of labour

Two persons in the Epidural group and 1 person in the Entonox group had pruritus.It was mild and only reassurance was needed. No patient in Epidural group had an incidence of dural or venous puncture. Four patients in the Entonox group and one patient in the epidural group had an incidence of nausea. Two patients in Epidural group had rigors transiently.

Seventeen patients with the Entonox group had drowsiness transiently when they were inhaling the gas but recovered in 2 to 3 minutes. No patient had an episode of hypotension in both groups. Urinary retention occurred in seven patients of Epidural group. Their bladder was emptied by simple catheterization. No patient had any episode of respiratory depression.

Eight patients in Entonox group complained of dry mouth which was treated with small sips of water.

SUMMARY

In this study the Epidural group offered better pain relief than the Entonox group. The Entonox group offered reasonable relief of pain in the first stage though its effectiveness was not good in the second stage.

Duration of labour, both the First stage and the Second stage were prolonged in the Epidural group than in the Entonox group. The total duration of labour was hence prolonged in the Epidural group.

Fetal outcome as assessed by the Apgar score at 1 minute and 5 minutes were comparable and all the babies were healthy in this study.

There was no appreciable fall in oxygen saturation in both groups, The incidence of side effects like urinary retention was more in the Epidural group and there were more incidence of nausea and Dryness of mouth in the Entonox group. Hemodynamics and respiratory rates were relatively higher in the Entonox group.

CONCLUSION

In our study we conclude that the Epidural technique offers better pain relief than Entonox gas. But it must be remembered that Entonox requires no special skill , easy to use, and safe. In many countries it is used by the midwives with one Doctor supervising.

We conclude that Entonox is a good, easy to use alternative to the Epidural technique. It can be used in conditions where skilled help is unavailable and where there may be contraindications to the Epidural Technique.

BIBLIOGRAPHY

1. Marx GF, Xatsnelson T. The introduction of nitrous oxide into obstetrics. *Obstetric Gynecology* 1992; 80:715-8. Nitrous oxide does not interfere with uterine activity.
2. Mills GH, Singh D, Longan M, et al. Nitrous oxide exposure on the labour ward. *Int J Obstet Anesth* 1996; 5:160-4.
3. Bernow J, Bjordal J, Wiklund KE. Pollution of delivery ward air by nitrous oxide: Effects of various modes of room ventilation, excess and close scavenging. *Acts Anaesthesiology Scand* 1984; 28:119-23.
4. Munley AJ, Railton R, Gray WM, Carter KB. Exposure of midwives to nitrous oxide in four hospitals. *BMJ* 1986; 293:1063-
5. Carstoniu I, Levytam S, Norman P, et al. Nitrous oxide in labour: Incidence of hypoxia Safety and efficacy assessed by a double-blind placebo controlled study. *Anesthesiology* 1994; 80:30-5.
6. Brownridge P. Treatment options for the relief of pain during childbirth. *Drugs* 1991; 41:69-80. With the intermittent inhalation of nitrous oxide, accumulation over time is negligible, and the neonate eliminates most of the gas within minutes of birth, principally by means of the lungs
7. Stefani SJ, Hughes SC, Shnider SM, et al. Neonatal neurobehavioral effects of inhalation analgesia for vaginal delivery. *Anesthesiology* 1982; 56:35 1-5 With the intermittent inhalation of nitrous oxide, nitrous oxide does not depress neonatal respiration or affect neonatal neurobehavior
8. TUNSTALL. ME. (1961) Use of a fixed nitrous oxide and oxygen mixture from one cylinder. *Lancet* 2, 964
9. Jevtovic todorovic SM, Mennerick et al Nitrous oxide is a NMDA antagonist *Nat Med* 4:460-3 1998
10. LANGLEY, Ga. (1987) Transcutaneous electrical nerve stimulation (TENS) and its relationship to placebo therapy: a review. *N. Z. Med.* 1. 100, 215—17.
11. HOLDCROFT. A. and MORGAN, M. (1974) An assessment of the analgesic effect in labour of pethidine and 50% nitrous oxide in oxygen (Entonox). 'I. *Obstetric. Gynaecology. Br. Commonwealth.* 81, 603—7
12. PHILIPS. K.C. and THOMAS. I.A. (1983) Second stage of labour with and without extradural analgesia. *Anaesthesia* 38. 972—6

13. Crawford JS. Lumbar epidural block in labour A clinical analysis. *Br. Anaesth* 1972; 44:66-74,
14. Thorp JA, Hu DH, Albin RM, et al. The effect of intrapartum epidural analgesia on nulliparous labor: A randomized, controlled, prospective trial. *Am J Obstetric Gynecology* 1993; 169:851-8.
15. .Burnstein R, Buddand R, Pickett JA. A survey of epidural analgesia for labour in the United Kingdom. *Anaesthesia* 1999; 54:634-4A)
16. Davies MW, Harrison IC, Ryan TDR. Current practice of epidural analgesia during normal labour. A survey of maternity units in the United Kingdom. *Anaesthesia* 1993; 48:63-5
17. Jackson A, Henry R, Avery N, et al. Informed consent *for* labour epidurals: What labouring women want *to* know *Can J Anaesth* 2000; 47:1068-73.
18. Chestnut DH, Weiner CP. Monitoring maternal heart rate during epidural injection of a test dose containing epinephrine (letter). *Anesthesiology* 1986; 64:839-40.
19. (a) Collins 1CM, Bevan DR, Beard RW. Fluid loading to reduce abnormalities of fetal heart rate and maternal hypotension during epidural analgesia in labour. *Br Med* 11978; 2:t460-l.
- (b) Ramanathan S. Masih A, Rock I, et al. Maternal and fetal effects of prophylactic hydration with crystalloids or colloids before epidural anesthesia. *Anesth Analg* 1983; 62:673-8.
20. Zamora JE, Rosaeg OP, Lindsay MP, et al. I-haemodynamic consequences and uterine contractions following 0.5 or 1.0 litre crystalloid infusion before obstetric epidural analgesia. *Can J Anaesth* 1996
21. Kinsella SM, Pirlet M, Mills MS, et a1. Randomized study of intravenous fluid preload before epidural analgesia during labour. *Br J Anaesth* 2000; 85:311-3.
22. Suonio S, Simpanen A-L, Olkkonen H, et al. Effect of the left lateral recumbent position compared with the supine and upright positions on placental blood flow in normal late pregnancy. *Ann Clin Ret* 1976; 8:22-6.
23. Ellington C, Katz VL, Watson WJ, et al. The effect of lateral tilt on maternal and fetal hemodynamnic variables. *Obstet Gynecol* 1991; 77:201-3.
24. Meister et al; A Comparison of Epidural Analgesia with 0.125% Ropivacaine with Fentanyl Versus 0.125% Bupivacaine with Fentanyl during Labor. *AJA* 2002; (18): 267-27 1.

25. M. Dresner Ropivacaine 0.2% versus bupivacaine 0.1% with fentanyl: a double blind comparison for analgesia during labour ; Br J Anaesth 2000; 85: 826—9.
26. Harrison RF, Shore M, Woods T, Mathews G, Gardiner J, Unwin AA comparative study of transcutaneous electrical nerve stimulation (TENS), entonox, pethidine + promazine and lumbar epidural for pain relief in labor. Acta Obstet Gynecol Scand. 1987;66(1):9-14.
27. Rosen MA. Nitrous oxide for relief of labor pain: a systematic review. Am J Obstet Gynecol 2002;186 (Suppl 5):S110-26
28. Benhamou D, Mercier FJ, Ben Ayed M, Auroy Y. Continuous epidural analgesia with bupivacaine 0.125% or bupivacaine 0.0625% plus sufentanil 0.25 microg.mL(-1): Int J Obstet Anesth. 2002 Jan;11(1):13-8
29. Su F, Wei X, Chen X, Hu Z, Xu H Clinical study on efficacy and safety of labor analgesia with inhalation of nitrous oxide in oxygen Zhonghua Fu Chan Ke Za Zhi. 2002 Oct;37(10):584-7.
30. Kilpatrick Si, Laros RK. Characteristics of normal labor. Obstet Gynecol 1989;74:85-7.
31. Sharma SK, Alexander IM, Messick G, et al. A randomized trial of epidural analgesia versus intravenous meperidine analgesia during labor in nulliparous women. Anesthesiology 2002; 96:546-51
32. Carstoniu J, Levytam S, Norman P, Daley D, Katz J, Sandler AN Nitrous oxide in early labor. Safety and analgesic efficacy assessed by a double-blind, lacebo-controlled study. Anesthesiology. 1994 Jan;80(1):30-5.
33. Clinical Anaesthesiology .G.EDWARD MORGAN. LANGE PUBLICATIONS 2002.
34. Wylie and Churchill Davidson : Practice of Anaesthesia :Vth edition. 1985
35. Ronald Miller Anaesthesia V edition 1999

PROFORMA
COMPARISON OF ENTONOX WITH EPIDURAL FOR LABOUR ANALGESIA

DATE	TIME	EPIDURAL(0.125 % Bupivacaine with 2 µgm/ml Fentanyl			
ENTONOX	NAME	AGE	Ht	Wt	IP NO

EDD

FHR

[illegible]

[illegible]

S NC NAME	AGE	HT	WT	ENTONOX	GEST AGE	CERV DIL	VAS 1	VAS 2	SENS	LOE	MAX	SEN	DUR I	DUR II	DUR III	TOTAL	DI	DEL	M	APGA	APGAR 5	TOTAL	SATISF
1 INDRA	24	150	50	38	5	3.55	8	67	45	158	30	13	193	NV	7	7	70						
2 LAKSMI	24	155	48	40	3	3.625	7.5	78	40	144	46	15	184	NV	8	10	70						
3 RANI	23	160	46	38	4	3.25	6.5	74	50	144	40	13	179	NV	7	10	30						
4 MARY	23	155	52	39	3	3.44	7	94	40	160	30	18	190	NV	8	9	60						
5 MANGALARA	21	152	45	40	5	3.125	8	94	45	142	26	20	184	NV	8	9	80						
6 ASIN	22	154	45	40	4	3.33	8	94	40	160	41	18	219	NV	7	9	30						
7 SAYIRA	21	156	50	39	3	3.75	5.5	83	40	160	38	20	172	NV	7	9	80						
8 MANGAMMA	20	148	49	38	4	2.5	7.5	94	40	146	40	15	201	NV	8	9	50						
9 SAKTHI	20	163	45	39	3	2	6.5	72	43	142	40	18	214	NV	7	9	70						
10 PUNITHA	22	160	45	39	5	3.5	7	72	45	170	26	14	224	OF	6	8	60						
11 SELVI	23	153	60	38	3	2.875	7	73	40	124	40	18	180	NV	8	9	70						
12 JEVALAKSHI	25	158	59	40	4	3.25	7	92	50	144	28	15	195	NV	7	9	70						
13 KAVITHA	22	164	52	39	3	3.625	7	92	50	146	42	16	176	NV	8	8	30						
14 SUMATHI	24	160	52	39	3	3.25	7.5	94	50	146	40	14	194	NV	8	10	60						
15 REKHA	26	156	59	38	3	2.875	6	75	45	154	28	14	162	NV	8	9	80						
16 HABIBA BI	24	150	49	40	3	3	7	75	45	124	44	16	215	NV	7	9	60						
17 MUMTAJ	22	148	52	39	4	2.75	7.5	85	45	156	45	18	197	NV	8	9	70						
18 RATHI	23	149	51	38	4	3.33	8	85	46	166	36	16	182	NV	8	9	70						
19 VIJAY	21	151	50	40	3	2.77	7	7	47	146	40	15	170	NV	8	10	90						
20 JAYABALA	24	157	49	40	3	3.25	7.5	7.2	48	148.1	37	16.2	191.8		7.45	9.1	63						
MEAN	22.7	154.95	50.6	39.1	3.6	3.15225	7.2		44.7	148.1	37	16.2	191.8		7.45	9.1	63						
SD	1.625455	4.860962	4.739531	0.852242	0.753937	0.429585	0.695852	3.743064		11.7065	6.496963	2.1667	17.22788		0.6	0.552506	16.89						

MASTER CHART																
S NC NAME	AGE	HT	EPIDURAL WT	GEST AGI CERV DIL VAS I	GROUP VAS 2	SENS LOS MAX SEN: DUR I	DUR II	DUR III	TOTAL DL DEL MAPGA APGAR 5	TOTAL SP						
1 SASIKALA	23	148	54	38	3	1	1.5	9	144	40	15	205 NV	7	9	90	
2 MAHESHWI	22	153	53	39	5	0.85	2	10	164	60	15	255 NV	8	10	80	
3 POONGODI	21	157	52	40	3	0.85	1	10	174	35	18	233 NV	7	9	80	
4 AMBIKA	21	158	50	40	4	0.85	1	11	158	50	20	234 NV	7	9	90	
5 DEVI	22	160	48	38	3	0.714	1	10	160	40	15	233 NV	8	10	80	
6 NASEENA	25	154	58	39	3	0.714	2	10	160	54	15	255 NV	7	9	70	
7 SUMATHI	20	155	54	39	4	0.714	2	9	158	54	20	258 NV	8	10	80	
8 SUJATHA	21	148	55	39	3	0.57	1	9	162	48	15	263 OF	6	9	70	
9 KANMANI	26	147	58	38	3	1	1	9	158	44	15	255 NV	7	10	70	
10 MYTHILI	20	148	48	38	3	1.125	1	9	184	45	18	233 NV	7	9	80	
11 SASIKALA	25	158	50	38	3	0.85	1	10	168	48	20	240 NV	7	9	90	
12 LAKSHMI	24	159	56	40	4	1.14	2	8	154	52	15	247 NV	8	9	90	
13 AMULU	23	159	55	40	3	1.42	1	9	168	62	15	232 NV	7	9	100	
14 BAVANI	21	155	48	38	3	1.42	2	8	174	48	20	268 NV	7	8	90	
15 NAFEEESA	19	155	50	39	4	0.714	1	9	164	48	20	246 NV	8	10	90	
16 CHITRA	22	157	54	38	3	1.25	1	10	200	52	20	LSCS	7	10	70	
17 KALAVANI	23	154	54	38	3	0.714	1	11	160	44	16	266 NV	7	10	90	
18 DEVI	22	157	49	38	3	0.85	1	11	170	54	18	250 NV	8	9	80	
19 LATHA	24	155	49	39	3	0.85	2	8	164	36	14	251 NV	7	9	80	
20 NIRMALA	22	148	48	39	5	1.28	2	10	170	36	14	228 NV	8	9	90	
MEAN	22.3	154.25	52.15	38.75	3.4	0.95805	1.5	9.9	165.7	46.5	17	248.75	7.3	9.3	83	
SD	1.838191	4.24109	3.375999	0.786398	0.680557	0.245036	0.492592	0.788069	0.410391	11.7029	7.324955	2.3446	15.74894	0.57	0.571241	8.645

PR EPI	PRO	PR5	PR10	PR15	PR30	PR45	PR60	PR78	PR120	PR150	PR180	PR2
1	110	116	100	78	80	80	90	76	92	84	80	
2	116	106	100	78	80	80	90	76	92	84	80	
3	88	116	89	80	90	77	95	80	81	92	78	
4	106	100	92	80	92	69	78	90	80	92	88	
5	96	90	84	72	74	92	66	92	72	72	92	
6	98	98	99	70	66	64	72	70	72	80	90	
7	102	106	92	84	72	73	70	85	65	81	79	
8	96	88	96	95	78	68	70	85	65	81	79	
9	106	98	100	88	95	72	68	69	94	80	88	
10	112	110	98	72	67	96	74	95	80	81	66	
11	98	98	94	78	78	67	78	90	66	66	69	
12	100	98	100	86	84	90	66	90	68	90	81	
13	99	98	100	86	84	90	66	90	68	90	81	
14	110	112	90	82	94	70	68	88	92	71	70	
15	102	98	95	78	68	80	78	84	90	91	85	
16	98	98	90	78	68	78	68	78	79	72	70	
17	106	98	100	68	72	73	71	66	64	74	77	
18	106	98	100	68	72	73	71	66	64	74	77	
19	96	90	88	81	92	75	74	92	74	77	74	
20	106	92	88	88	84	82	80	78	77	80	90	
Mean	102.55	100.5	94.65	79.45	80.85	78.95	76.4	80.85	80.25	81.45	79.65	78.45
SD	6.739319	8.15314	5.163383	6.731505	9.64788	9.912645	10.86472	9.767158	9.546975	8.029387	8.797577	6.94698

PR	ENTO	PR0	PR5	PR10	PR15	PR30	PR45	PR60	PR78	PR120	PR150	PR180	PR2
1	100	98	90	85	98	90	88	85	90	100	112	1	
2	106	72	100	100	77	100	77	92	98	110	110	1	
3	106	72	105	110	77	106	87	100	87	116	114	1	
4	106	98	100	100	100	100	89	92	98	96	106	1	
5	106	106	100	88	95	100	98	86	85	106	96	1	
6	118	116	106	98	100	99	88	87	90	78	114	1	
7	96	90	88	88	86	80	80	78	80	105	106	1	
8	98	98	99	89	88	86	78	98	88	106	108	1	
9	102	98	100	102	98	100	89	92	88	106	110	1	
10	106	98	100	100	100	100	89	92	98	100	94	1	
11	98	98	90	101	98	90	88	86	90	94	108	1	
12	98	98	100	100	98	90	88	86	102	110	96	1	
13	99	98	88	98	86	88	85	88	86	110	88	1	
14	110	112	86	100	86	106	86	102	99	120	112	1	
15	102	92	95	92	103	85	92	102	92	109	109	1	
16	98	98	100	86	100	100	86	92	92	94	110	1	
17	106	98	100	100	100	100	89	92	98	107	96	1	
18	120	112	100	100	100	106	100	102	99	96	116	1	
19	98	98	100	102	103	98	96	102	105	96	112	1	
20	98	96	88	87	75	89	88	85	94	110	110	1	
Mean	103.55	97.3	96.75	96.3	93.4	95.65	88.05	91.95	92.95	103.45	106.35	9	
SD	6.637017	10.82444	6.086006	6.906138	9.184655	7.679604	5.762629	7.044782	6.468344	9.41709	7.8892	3.9336	

SBP EPI	SBP0	SBP5	SBP10	SBP15	SBP30	SBP45	SBP60	SBP90	SBP120	SBP150	SBP180	SBP240
1	118	122	110	106	104	106	120	106	110	116	114	114
2	122	136	122	114	110	116	106	108	108	110	124	1
3	132	132	110	106	110	116	112	116	106	112	120	1
4	120	112	116	100	100	110	110	136	114	130	118	1
5	120	110	114	102	116	102	120	116	106	108	104	1
6	136	110	134	110	106	106	116	106	120	116	120	1
7	122	110	110	106	106	122	114	134	108	110	124	1
8	124	110	124	110	108	108	110	118	110	110	110	1
9	126	118	105	110	108	106	120	120	108	106	128	1
10	130	132	120	110	108	118	120	116	120	124	116	1
11	130	120	110	120	114	104	126	118	106	112	120	1
12	132	128	110	110	116	118	112	120	118	130	120	1
13	120	110	120	122	124	120	118	114	130	132	120	1
14	132	136	126	120	118	110	124	122	130	120	126	1
15	122	116	110	116	106	124	118	124	108	110	118	1
16	124	110	134	110	108	118	110	118	118	110	102	1
17	112	110	106	110	110	106	105	112	114	112	110	1
18	122	136	108	122	112	108	120	126	108	110	108	1
19	132	132	110	110	110	116	112	120	114	118	110	1
20	120	112	116	100	100	116	110	116	116	130	116	1
Mean	124.8	120.1	115.75	110.7	109.7	112.5	115.15	118.3	113.6	116.3	116.4	116
SD	6.169535	10.55263	8.644286	6.657801	5.849876	6.581473	5.869412	7.821024	7.329824	8.442374	7.155418	5.7041

SBP ENT	SBP0	SBP5	SBP10	SBP15	SBP30	SBP45	SBP60	SBP90	SBP120	SBP150	SBP180	SBP24
1	136	108	134	116	116	120	126	120	130	128	138	
2	122	110	106	106	110	122	136	130	108	138	132	
3	124	110	112	110	110	108	110	116	126	128	128	
4	124	112	114	110	110	110	108	136	116	110	136	
5	120	110	112	106	136	110	120	130	120	138	120	
6	132	110	130	110	106	110	116	106	118	124	130	
7	124	110	132	110	110	108	118	118	120	128	130	
8	128	118	105	110	106	106	120	118	108	132	132	
9	132	130	118	110	108	114	120	120	120	130	128	
10	134	120	110	130	128	104	126	122	120	130	120	
11	132	128	110	124	116	124	112	120	124	120	132	
12	122	110	120	118	124	118	118	118	120	130	118	
13	120	110	106	118	110	106	118	112	114	128	114	
14	124	136	108	118	112	118	120	126	118	136	132	
15	130	132	110	118	110	116	118	120	118	130	130	
16	124	120	110	124	130	104	124	118	124	122	132	
17	132	124	110	110	124	118	112	120	124	134	124	
18	132	110	112	122	124	112	118	114	120	120	128	
19	120	110	114	102	136	102	120	132	120	120	130	
20	132	136	130	120	118	110	124	122	120	130	128	
Mean	127.2	117.7	115.15	114.6	117.2	112	119.2	120.9	119.4	127.8	128.1	117
SD	5.287523	9.84672	9.17247	7.257664	9.741933	6.423641	6.304551	7.09262	5.275564	6.894697	6.068903	7.297

<u>DBP EPI</u>	<u>DBP 0</u>	<u>DBP5</u>	<u>DBP10</u>	<u>DBP15</u>	<u>DBP30</u>	<u>DBP45</u>	<u>DBP60</u>	<u>DBP90</u>	<u>DBP120</u>	<u>DBP150</u>	<u>DBP180</u>	<u>DBP240</u>
1	88	84	82	64	66	65	70	70	70	72	70	
2	88	86	78	70	68	66	60	64	70	66	68	
3	82	80	78	72	70	72	66	72	68	66	70	
4	86	84	84	82	64	72	74	68	70	70	68	
5	88	86	82	70	80	70	68	76	70	82	84	
6	90	84	80	68	66	74	76	66	70	76	76	
7	86	82	74	70	66	66	86	68	68	70	70	
8	88	80	68	64	66	86	72	88	78	78	80	
9	86	82	72	70	72	74	68	68	72	78	74	
10	80	76	70	72	74	82	86	82	74	74	70	
11	86	82	80	80	74	74	74	74	84	78	82	
12	78	82	74	74	82	70	68	66	72	74	78	
13	80	80	88	86	66	70	82	72	82	88	74	
14	82	80	90	70	72	72	66	82	66	72	82	
15	80	78	78	66	84	84	80	78	76	76	82	
16	76	72	70	66	74	74	66	68	72	70	78	
17	86	78	70	88	80	82	88	82	80	78	70	
18	84	84	76	82	74	76	82	74	82	78	82	
19	88	78	74	78	82	70	78	66	72	78	66	
20	74	70	72	74	74	72	70	70	68	70	72	
Mean	83.8	80.4	77	73.3	72.7	73.55	74	72.7	73.2	74.7	74.8	74
SD	4.537563	4.235191	6.138747	7.116327	6.266872	5.898037	7.947194	6.689347	5.327189	5.40078	5.782005	5.3469

DBP ENT	DBP 0	DBP5	DBP10	DBP15	DBP30	DBP45	DBP60	DBP90	DBP120	DBP150	DBP180	DBP210
1	80	90	88	94	66	70	70	72	70	74	88	
2	66	80	90	70	90	72	66	72	66	88	88	
3	76	88	78	76	88	74	76	84	80	86	86	
4	82	72	84	74	64	74	74	78	80	74	88	
5	86	86	84	82	80	86	82	76	70	90	82	
6	82	86	84	70	80	86	68	76	70	82	90	
7	82	76	82	88	82	82	86	68	74	86	88	
8	78	74	90	88	74	86	72	74	78	88	90	
9	76	82	72	76	84	82	76	68	76	88	88	
10	74	76	86	88	82	80	86	68	74	86	74	
11	74	66	90	82	80	86	72	82	82	78	88	
12	68	82	72	80	84	84	68	68	74	86	74	
13	66	72	74	70	70	72	74	80	82	88	80	
14	82	78	70	72	80	82	80	82	70	86	88	
15	78	82	76	86	74	76	74	74	74	90	86	
16	84	78	74	84	82	70	84	66	76	88	88	
17	84	72	84	80	64	74	80	78	80	88	88	
18	84	86	80	82	80	86	80	76	80	82	84	
19	86	86	80	70	80	86	80	76	80	78	84	
20	86	80	82	84	72	74	74	76	76	88	88	
Mean	78.7	79.6	81	79.8	77.8	79.1	76.1	74.7	75.6	84.2	85.3	74.3
SD	6.432647	6.410518	6.37429	7.25186	7.452304	6.137889	5.963927	5.242539	4.66115	5.146281	4.824281	4.467426

MBP EPI	MBP 0	MBP5	MBP10	MBP15	MBP30	MBP45	MBP60	MBP90	MBP120	MBP150	MBP180	MBP240
1	98	96.66667	91.33333	78	78.66667	78.66667	86.66667	82	83.33333	86.66667	84.66667	86.66667
2	99.33333	102.6667	92.66667	84.66667	82	82.66667	75.33333	78.66667	82.66667	80.66667	86.66667	86.66667
3	98.66667	97.33333	88.66667	83.33333	83.33333	86.66667	81.33333	86.66667	80.66667	81.33333	86.66667	86.66667
4	97.33333	93.33333	94.66667	88	76	84.66667	86	90.66667	84.66667	90	84.66667	91.33333
5	98.66667	94	92.66667	80.66667	92	80.66667	85.33333	89.33333	82	90.66667	90.66667	8
6	105.3333	92.66667	98	82	79.33333	84.66667	89.33333	79.33333	86.66667	89.33333	90.66667	8
7	98	91.33333	86	82	79.33333	84.66667	95.33333	90	81.33333	83.33333	88	83.3333
8	100	90	86.66667	79.33333	80	93.33333	84.66667	98	88.66667	88.66667	90	86.6666
9	99.33333	94	83	83.33333	84	84.66667	85.33333	85.33333	84	87.33333	92	83.3333
10	96.66667	94.66667	86.66667	84.66667	85.33333	94	97.33333	93.33333	89.33333	90.66667	85.33333	83.3333
11	100.6667	94.66667	90	93.33333	87.33333	84	91.33333	88.66667	91.33333	89.33333	94.66667	92.66667
12	96	97.33333	86	86	93.33333	86	82.66667	84	87.33333	92.66667	92	93.3333
13	93.33333	90	98.66667	98	85.33333	86.66667	94	86	98	102.6667	89.33333	90.66667
14	98.66667	98.66667	102	86.66667	87.33333	84.66667	85.33333	87.33333	88	96.66667	91.33333	90.66667
15	94	90.66667	88.66667	82.66667	91.33333	97.33333	92.66667	93.33333	86.66667	87.33333	94	94
16	92	84.66667	91.33333	80.66667	85.33333	88.66667	80.66667	84.66667	87.33333	83.33333	86	89.33333
17	94.66667	88.66667	82	95.33333	90	90	93.66667	92	91.33333	89.33333	83.33333	90
18	96.66667	101.3333	86.66667	95.33333	86.66667	85.33333	89.33333	84	91.33333	90.66667	91.33333	90
19	102.6667	96	86	88.66667	91.33333	86.66667	83.33333	85.33333	86	91.33333	80.66667	89.33333
20	89.33333	84	86.66667	82.66667	82.66667	86.66667	83.33333	85.33333	84	90	86.66667	92
SD	3.655326	4.867724	5.289154	5.711483	4.95467	4.425338	5.78289	5.192324	4.18295	4.670556	4.103914	3.760522
MEAN	97.46667	93.63333	89.91667	85.76667	85.03333	86.53333	87.71667	87.9	86.66667	88.56667	88.66667	88.23333

MBP ENT	MBP 0	MBP5	MBP10	MBP15	MBP30	MBP45	MBP60	MBP90	MBP120	MBP150	MBP180	MBP240
1	98.66667	96	103.3333	101.3333	82.66667	86.66667	88.66667	88	90	92	104.6667	88.66667
2	84.66667	90	95.33333	82	96.66667	88.66667	89.33333	91.33333	80	104.6667	102.6667	97.33333
3	92	95.33333	89.33333	87.33333	95.33333	85.33333	87.33333	94.66667	95.33333	100	100	86.66667
4	96	85.33333	94	86	79.33333	86	85.33333	97.33333	92	86	104	88.66667
5	97.33333	94	93.33333	90	98.66667	94	94.66667	94	86.66667	106	94.66667	92.66667
6	98.66667	94	99.33333	83.33333	88.66667	94	84	86	86	96	103.3333	80.66667
7	96	87.33333	98.66667	95.33333	91.33333	90.66667	96.66667	84.66667	89.33333	100	102	82.66667
8	94.66667	88.66667	95	95.33333	84.66667	92.66667	88	88.66667	88	102.6667	104	87.33333
9	94.66667	98	87.33333	87.33333	92	92.66667	90.66667	85.33333	90.66667	102	101.3333	83.33333
10	94	90.66667	94	102	97.33333	88	99.33333	86	89.33333	100.6667	89.33333	85.33333
11	93.33333	86.66667	96.66667	96	92	98.66667	85.33333	94.66667	96	92	102.6667	90.66667
12	86	91.33333	88	92.66667	97.33333	95.33333	84.66667	84.66667	89.33333	100.6667	88.66667	89.33333
13	84	84.66667	84.66667	86	83.33333	83.33333	88.66667	90.66667	92.66667	101.3333	91.33333	86
14	96	97.33333	82.66667	87.33333	90.66667	94	93.33333	96.66667	86	102.6667	102.6667	90
15	95.33333	98.66667	87.33333	96.66667	86	89.33333	88.66667	89.33333	88.66667	103.3333	100.6667	95.33333
16	97.33333	92	86	97.33333	98	81.33333	97.33333	83.33333	92	92.66667	102.6667	91.33333
17	100	89.33333	92.66667	90	84	88.66667	90.66667	92	94.66667	103.3333	94.66667	89.33333
18	100	94	90.66667	95.33333	94.66667	94.66667	92.66667	88.66667	93.33333	94.66667	101.3333	92
19	97.33333	94	91.33333	80.66667	98.66667	91.33333	93.33333	94.66667	93.33333	92	99.33333	92
20	101.3333	98.66667	98	96	87.33333	86	90.66667	91.33333	90.66667	102	101.3333	88.66667
SD	4.908994	4.398166	5.417402	6.26099	6.115459	4.484673	4.342635	4.294836	3.796582	5.424227	4.994853	4.122537
MEAN	94.86667	92.3	92.38333	91.4	90.93333	90.06667	90.46667	90.1	90.2	98.73334	99.56667	88.9

RR EPI	RR0	RR5	RR10	RR15	RR30	RR45	RR60	RR90	RR120	RR150	RR180	RR240
1	24	24	20	16	20	16	20	16	20	18	14	19
2	22	21	20	18	16	20	15	16	20	18	17	16
3	20	20	18	18	20	20	18	18	20	17	17	17
4	23	19	17	20	18	16	20	18	17	20	14	15
5	18	19	21	20	19	19	18	18	20	20	16	15
6	18	22	18	18	16	16	15	15	20	16	14	15
7	22	23	18	21	18	17	16	20	14	12	16	14
8	19	21	18	15	15	20	14	16	16	14	15	14
9	21	20	20	20	18	18	20	21	20	15	16	18
10	23	24	20	18	16	16	20	15	15	20	18	16
11	23	23	18	18	20	16	17	16	16	17	17	18
12	21	20	19	19	20	19	18	19	19	19	18	18
13	23	19	19	20	21	22	21	18	20	20	20	19
14	21	20	20	19	22	18	17	17	19	18	19	18
15	24	23	18	20	19	22	23	18	21	20	18	18
16	19	22	19	18	19	18	17	15	18	15	20	19
17	24	23	18	15	17	16	18	17	18	17	18	15
18	23	22	19	18	19	19	17	17	17	16	19	20
19	20	19	22	19	19	22	18	21	16	17	17	19
20	18	19	22	21	22	19	19	19	21	17	18	20
Mean	21.3	21.15	19.2	18.55	18.7	18.45	18.05	17.5	18.35	17.3	17.05	17.15
SD	2.105132	1.785173	1.399248	1.731291	1.976174	2.114486	2.21181	1.849609	2.109502	2.226633	1.848897	1.980829

RR ENT	RR0	RR5	RR10	RR15	RR30	RR45	RR60	RR90	RR120	RR150	RR180	RR240
1	22	24	23	20	19	21	20	20	20	20	24	19
2	20	21	22	22	23	20	22	22	20	23	24	22
3	18	20	18	23	18	20	23	22	20	24	26	21
4	23	18	22	24	19	24	20	22	21	20	24	24
5	23	24	23	22	24	21	24	18	19	24	20	22
6	20	21	21	23	18	23	24	18	20	19	24	20
7	24	22	23	19	18	18	21	24	18	24	24	18
8	21	20	20	23	18	19	18	20	20	24	26	21
9	23	23	18	22	20	18	20	24	19	23	24	22
10	18	22	18	24	23	16	24	22	24	24	18	23
11	22	22	24	21	23	20	20	20	18	20	24	22
12	18	21	22	23	21	23	20	22	21	24	20	19
13	22	18	17	18	19	19	17	16	16	23	18	19
14	22	23	18	22	24	21	22	24	20	26	24	22
15	24	22	21	20	21	21	20	22	23	24	24	20
16	25	19	22	20	19	22	20	21	24	20	23	19
17	18	19	20	21	22	20	23	19	20	26	18	22
18	20	18	20	21	18	21	24	18	24	22	26	20
19	24	24	24	24	21	20	21	24	18	24	26	21
20	23	23	18	23	22	20	18	20	24	26	24	20
SD	2.259483	2.041671	2.250146	1.712954	2.164304	1.871532	2.139233	2.314713	2.305029	2.15211	2.704285	1.576138
Mean	21.5	21.2	20.7	21.75	20.5	20.35	21.05	20.9	20.45	23	23.05	20.8

VAS EPI	VAS0	VAS5	VAS10	VAS15	VAS30	VAS45	VAS60	VAS90	VAS120	VAS150	VAS180	VAS210
1	9	8	3	2	0	1	0	1	2	1	2	
2	10	8	4	2	0	1	1	1	0	1	2	
3	8	7	3	2	0	1	1	1	0	1	2	
4	9	7	3	2	0	1	1	0	1	1	1	
5	10	8	2	1	1	1	0	0	1	1	1	
6	8	7	3	1	1	0	1	1	2	1	1	
7	9	8	2	1	0	1	1	0	1	1	2	
8	10	8	3	1	1	0	1	1	0	1	2	
9	8	7	5	2	1	1	0	1	1	1	1	
10	9	7	4	2	1	0	1	1	1	2	1	
11	10	7	4	3	0	1	0	1	1	1	2	
12	8	8	3	2	1	1	1	0	0	1	1	
13	9	8	4	2	1	0	1	2	1	1	2	
14	9	8	5	3	2	2	1	1	1	1	1	
15	10	8	4	1	0	1	1	0	1	2	2	
16	9	7	4	2	1	1	0	1	1	1	1	
17	8	7	3	1	1	0	0	1	1	2	2	
18	8	7	4	2	1	0	0	1	1	1	1	
19	9	7	3	1	0	1	1	0	1	1	1	
20	10	8	3	2	2	1	1	2	1	0	2	
Mean	9	7.5	3.45	1.75	0.7	0.75	0.7	0.75	0.9	1.1	1.5	1.263158
SD	0.794719	0.512989	0.825578	0.638666	0.656947	0.55012	0.571241	0.71635	0.552506	0.447214	0.512989	0.452414

VAS ENT	VAS0	VAS5	VAS10	VAS15	VAS30	VAS45	VAS60	VAS90	VAS120	VAS150	VAS180	VAS240
1	10	4	5	4	3	4	3	3	2	4	8	
2	9	4	4	3	3	4	3	4	4	8	7	
3	8	3	3	4	3	3	3	3	4	6	7	
4	9	4	5	3	4	2	3	3	3	3	7	
5	10	4	3	3	3	2	3	3	4	8	2	
6	9	4	3	3	2	4	3	3	4	4	8	
7	9	4	5	4	4	3	3	4	3	5	6	
8	10	3	2	2	3	2	2	2	4	7	8	
9	8	3	2	2	1	1	2	3	2	6	7	
10	9	3	4	3	4	3	4	3	4	8	7	
11	8	3	3	3	4	3	3	3	2	3	4	
12	8	3	3	3	4	3	3	2	2	7	2	
13	10	4	4	4	3	4	3	4	4	7	3	
14	10	3	3	2	2	3	4	4	3	7	2	
15	8	2	2	3	2	2	2	1	3	8	7	
16	10	3	3	2	3	3	3	2	5	6	6	
17	9	2	2	2	3	3	4	3	3	3	7	
18	8	2	2	2	3	3	3	3	4	8	7	
19	7	3	2	3	3	3	4	3	5	5	8	
20	10	3	3	4	3	2	2	3	4	3	7	
Mean	8.95	3.2	3.2	3	2.95	2.95	3	2.9	3.5	5.85	6.25	
SD	0.944513	0.695852	1.005249	0.725476	0.759155	0.825578	0.648886	0.718185	0.888523	1.954078	1.915999	

FHR EPI	FHR0	FHR5	FHR10	FHR15	FHR30	FHR45	FHR60	FHR90	FHR120	FHR150	FHR180	FHR240
1	120	145	132	125	129	128	131	144	152	139	127	14
2	130	124	144	128	128	132	144	116	140	140	140	14
3	120	136	138	140	140	146	136	134	136	145	132	12
4	125	136	134	142	132	130	130	136	140	140	136	14
5	126	132	134	136	136	140	140	140	130	126	130	13
6	132	120	130	140	140	130	130	140	130	126	130	12
7	132	120	132	140	140	130	130	136	134	136	140	13
8	140	136	140	132	140	130	142	132	144	126	144	13
9	123	136	140	132	132	140	130	130	140	126	144	13
10	126	132	140	132	136	140	130	132	140	140	130	13
11	120	136	140	140	130	126	136	136	130	140	140	14
12	130	140	142	140	130	140	140	136	130	140	140	14
13	126	130	140	140	130	140	136	140	136	142	144	14
14	136	130	140	140	130	140	130	140	136	142	144	14
15	128	140	136	134	136	136	140	136	140	140	140	14
16	134	130	134	136	130	130	140	136	140	140	140	14
17	136	136	136	130	140	140	140	140	140	140	140	14
18	120	136	140	136	140	140	140	140	140	140	140	14
19	136	136	140	136	140	140	136	136	140	140	136	136
20	128	136	140	140	136	144	144	144	140	130	130	136
Mean	128.4	133.35	137.6	135.85	134.25	135.7	136.75	136	137.3	136.1	136.55	135.35
SD	6.116414	6.360031	3.81686	4.901933	4.563874	5.629808	4.972292	5.98243	5.704107	5.533629	5.083254	5.546692

FHR	ENTO	FHR0	FHR5	FHR10	FHR15	FHR30	FHR45	FHR60	FHR90	FHR120	FHR150	FHR180	FHR240
1	136	140	140	140	140	130	136	140	136	144	136	140	130
2	128	124	136	136	136	140	14	130	130	136	136	142	130
3	130	124	144	128	128	128	132	144	116	140	140	140	120
4	126	136	136	132	132	140	140	130	130	140	130	140	130
5	132	136	140	136	136	140	140	130	136	136	140	136	140
6	128	138	136	136	136	140	132	132	136	144	142	136	140
7	132	120	132	140	140	140	130	142	132	144	126	144	130
8	136	136	140	140	140	136	140	140	136	136	136	144	136
9	132	136	136	136	140	140	140	136	136	142	136	142	140
10	136	140	136	140	140	136	142	136	126	142	142	144	140
11	136	140	136	140	140	136	140	130	130	140	136	140	140
12	120	136	140	136	136	140	140	140	136	140	140	136	136
13	132	120	130	140	140	140	130	130	136	134	136	140	132
14	126	132	134	136	136	136	140	140	140	130	126	130	126
15	120	136	138	140	140	140	146	136	134	136	145	132	142
16	128	130	140	136	136	130	140	140	132	130	130	142	140
17	136	136	140	130	130	140	130	140	130	140	136	132	140
18	126	142	136	140	140	136	140	142	136	142	142	136	134
19	126	136	136	138	138	140	140	140	130	130	136	136	134
20	136	130	136	130	130	140	130	140	140	140	136	130	140
Mean	130.1	133.4	137.1	136.7	137.4	131.1	136.9	132.9	138.3	136.35	138.1	135.6	
SD	5.16975	6.652265	3.210181	3.908156	3.898718	27.98101	4.833001	5.40857	4.600915	5.163383	4.564162	6.210348	

SPO2 EPI	SPO20	SPO25	SPO210	SPO215	SPO230	SPO245	SPO260	SPO290	SPO2120	SPO2150	SPO2180	SPO2240
1	99	98	97	99	99	100	99	98	100	100	98	100
2	100	96	98	97	100	97	100	97	98	97	98	100
3	100	96	98	97	100	98	97	98	96	98	98	99
4	100	96	95	96	98	97	99	99	99	100	100	100
5	100	96	98	98	99	99	99	99	99	100	100	100
6	96	99	99	99	98	99	99	99	96	97	98	99
7	96	97	99	99	98	96	97	95	99	98	98	98
8	100	98	99	97	100	99	99	100	99	98	96	96
9	100	99	98	97	96	98	96	99	99	98	97	96
10	99	96	96	97	96	98	99	98	97	96	96	96
11	97	99	98	98	97	100	100	100	98	98	97	96
12	100	100	100	96	95	96	96	96	98	98	97	96
13	98	97	98	100	98	99	98	99	99	99	96	96
14	98	100	98	98	99	100	100	99	99	99	96	98
15	99	97	98	99	98	99	99	99	100	99	99	98
16	100	98	98	98	98	98	98	98	98	100	100	100
17	98	100	99	98	97	96	98	98	98	99	99	99
18	97	100	98	99	98	96	98	97	96	99	99	98
19	98	98	99	100	100	98	99	98	97	96	98	98
20	98	98	98	98	98	97	99	99	100	98	98	99
Mean	98.65	97.9	98	98.04762	98.1	98	98.4	98.25	98.25	98.1	98	98.2
SD	1.386969	1.48324	1.076055	1.145931	1.410487	1.376494	1.187656	1.292692	1.292692	1.252366	1.414214	1.361114

SPO2 ENT	SPO20	SPO25	SPO210	SPO215	SPO230	SPO245	SPO260	SPO290	SPO2120	SPO2150	SPO2180	SPO2240
1	100	99	98	99	98	97	96	98	99	96	96	96
2	99	97	98	99	98	98	98	98	99	98	98	98
3	100	98	98	98	98	99	98	98	99	98	98	98
4	98	100	99	98	97	96	98	98	98	99	99	99
5	97	100	98	99	98	96	98	98	99	98	99	98
6	98	98	99	100	100	96	98	97	96	99	98	98
7	100	96	95	96	98	97	99	98	97	96	98	99
8	100	96	98	98	99	99	99	99	99	100	100	99
9	96	99	99	99	98	99	99	99	96	97	98	98
10	100	98	96	98	99	96	97	95	99	98	96	96
11	100	96	95	96	98	97	98	99	99	98	99	98
12	100	96	98	98	99	99	99	99	99	100	100	99
13	96	99	99	99	98	96	97	99	96	97	98	98
14	96	97	98	99	100	99	97	95	99	98	96	96
15	100	98	99	97	96	98	99	100	99	98	97	96
16	100	99	98	98	96	98	96	99	97	96	96	98
17	99	96	96	98	97	100	100	98	98	98	97	96
18	98	98	99	100	100	98	99	98	97	96	98	96
19	100	96	95	96	98	97	99	99	99	100	100	99
20	100	96	98	98	99	99	99	99	96	97	98	98
Mean	98.85	97.6	97.65	98.1	98.2	97.7	98.3	98.25	97.95	97.85	97.9	97.7
SD	1.531253	1.429022	1.424411	1.209611	1.151658	1.218282	1.080935	1.332785	1.234376	1.308877	1.333772	1.218282

	SENS EPI	SENS0	SENS5	SENS10	SENS15	SENS30	SENS45	SENS90	SENS120	SENS180	SENS240
	1			10	9	9	10	10	9	10	11
	2			9	9	8	8	9	10	10	10
	3			9	9	9	8	8	10	10	11
	4			9	9	8	9	9	10	10	11
	5			9	9	9	8	9	10	11	11
	6			10	9	8	9	8	10	10	11
	7			9	9	9	9	9	9	10	11
	8			8	9	8	8	9	10	10	11
	9			9	9	8	8	8	10	10	11
	10			9	10	9	9	9	10	10	11
	11			9	9	8	8	9	10	10	11
	12			9	10	8	10	9	10	11	11
	13			9	9	9	8	8	10	10	11
	14			9	9	8	8	9	10	10	11
	15			9	9	8	8	9	9	10	11
	16			9	8	8	8	9	10	10	11
	17			9	9	8	8	9	10	10	11
	18			9	10	8	8	9	10	11	11
	19			9	9	8	8	9	9	10	10
	20			9	10	9	9	9	10	10	11
Mean				9.05	9.15	8.35	8.45	8.85	9.8	10.15	10.85
SD				0.394034	0.48936	0.48936	0.686333	0.48936	0.410391	0.366348	0.366348

ENTO	DURAL PL	VENOUS F	NAUSEA	Drowsy	PRURITUS	RIGORS	HYPOTEN	URINARY	RESPIRAT	DRYNESS OF MOUTH
1			NAUSEA	y n	n	n	n	n	n	n
2			n	y n	n	n	n	n	y	
3			NAUSEA	y n	n	n	n	n	n	
4			NAUSEA	n n	n	n	n	n	n	
5			n	y n	n	n	n	n	y	
6			n	y n	n	n	n	n	n	
7			n	y n	n	n	n	n	y	
8			n	y n	n	n	n	n	y	
9			n	y n	n	n	n	n	n	
10			n	n n	n	n	n	n	n	
11			n	y n	n	n	n	n	y	
12			n	y n	n	n	n	n	n	
13			n	y n	n	n	n	n	y	
14			n	y n	n	n	n	n	n	
15			NAUSEA	y n	n	n	n	n	n	
16			n	n n	n	n	n	n	n	
17			n	y n	n	n	n	n	y	
18			n	y n	n	n	n	n	n	
19			n	y n	n	n	n	n	n	
20			n	y n	n	n	n	n	y	